DOI:
10.1097/CCM.0000000000002961

Document Version
Peer reviewed version

Incidence and outcomes for patients with cirrhosis admitted to United Kingdom critical care units

Mark JW McPhail[1] PhD, Francesca Parrott[2] PhD, Julia A Wendon[1] MD, David A Harrison[2] PhD, Kathy A Rowan[2] PhD and William Bernal[1] MD

1 Liver Intensive Therapy Unit, Institute of Liver Studies, King's College Hospital, Denmark Hill, London

2 Intensive Care National Audit & Research Centre, London

THIS IS THE ACCEPTED AND NOT PUBLISHED VERSION

Keywords - intensive care; mortality; acute-on-chronic liver failure; liver failure; prognosis; organ support; ICNARC

Corresponding author

Dr William Bernal
Liver Intensive Therapy Unit
Institute of Liver Studies
Kings College Hospital
Denmark Hill
London SE5 9RS
Tel: +020 3299 3367
Fax: +44 203 299 3167
william.bernal@kcl.ac.uk

List of abbreviations

ACLF acute on chronic liver failure
ARLD Alcohol related liver disease
APACHE Acute Physiology and Chronic Health Evaluation
CCMDS critical care minimal data set
CMP Case Mix Programme
CCU critical care unit
CLIF chronic liver failure
HDU high dependency unit
ICNARC Intensive Care National Research Centre
ICU intensive care unit
SOFA sequential organ failure assessment

Author contributions

Designed the study MM, KR, WB
Analysed the data FP, DH, KR
Interpreted the data MM, JW, WB, FP, DH
Wrote the manuscript MM, FP, DH, KR, JW, WB
Guarantor WB

Financial Support

MJWM is grateful to the Wellcome Trust, UK for support in the form of a Postdoctoral Research Training Fellowship during part of the period in which this article was produced. He is also grateful to the NIHR Biomedical Research Centres at both Imperial College London and Kings College London for infrastructure support.

Conflicts of interest

The authors have no conflicts of interest relevant to this manuscript.

ABSTRACT

Objective: To assess the epidemiology and outcome of patients with cirrhosis following critical care unit (CCU) admission.

Design: Retrospective cohort study.

Setting: CCUs in England, Wales and Northern Ireland participating in the United Kingdom Intensive Care National Audit and Research Centre (ICNARC) Case Mix Programme (CMP)

Patients 31,363 patients with cirrhosis identified out of 1,168,650 total CCU admissions (2.7%) admitted to UK CCUs between 1998 and 2012.

Interventions: none

Measurements and main results: 10,936 patients had alcohol-related liver disease (ARLD, 35%). 1.6% of CCU admissions in 1998 had cirrhosis rising to 3.1% in 2012. The crude CCU mortality of patients with cirrhosis was 41% in 1998 falling to 31% in 2012 ($p<0.001$). Crude hospital mortality fell from 58% to 46% over the study period ($p<0.001$). Mean(SD) APACHE II score in 1998 was 20.3(8.5) and 19.5(7.1) in 2012. Mean APACHE II score for patients with ARLD in 2012 was 20.6(7.0) and 19.0(7.2) for non-ARLD ($p<0.001$). In adjusted analysis ARLD was associated with increased risk of death (Odds ratio(OR) 1.51 (95%CI 1.42-1.62, $p<0.001$) with a year-on-year reduction in hospital mortality (adjusted-OR 0.95/yr, (0.94-0.96, $p<0.001$)).

Conclusions: More patients with cirrhosis are being admitted to CCUs but with increasing survival rates. Patients with ARLD have reduced survival rates partly explained by higher levels of organ failure on admission. Patients with cirrhosis and organ failure warrant a trial of organ support and universal prognostic pessimism is not justified.

INTRODUCTION

The incidence of liver cirrhosis is rising worldwide with expected increases in hospital admissions and liver-related deaths (1, 2). Patients with cirrhosis are prone to decompensation and extra-hepatic organ failure, requiring hospital treatment and admission to the critical care unit (CCU), with high short-term mortality (3) and significant economic cost (4, 5).

Studies describing the mortality of critically-ill patients with cirrhosis suggest overall mortality ranges between 40 and 80%, with a progressive increase dependent upon the number of organ systems failing (6-9). Earlier reports noted that more than 80% of patients with 2 or more organs in failure by the third day of CCU admission did not survive to hospital discharge(7).

Marked improvements in survival have been noted in patients with acute decompensation (AD) of cirrhosis and organ failure admitted to specialist liver transplant (LT) centres (10, 11) over the last decade. This improvement can partly be explained by reductions in admission organ failure scores as patients were admitted earlier during their critical illness. In cohorts from the Royal Free Hospital, London(10) and King's College Hospital, London(11) the aetiology of underlying cirrhosis was not associated with a survival difference. Furthermore, patients admitted following gastrointestinal haemorrhage had lower mortality rates compared to those with multi-organ failure. Patients with cirrhosis and significant acute organ dysfunctions have recently been classified by international consensus as suffering from the distinct clinical entity of acute-on-chronic liver failure (ACLF)(3).

The background survival for all-comers admitted to CCUs has been increasing for many years. In the United Kingdom, the present expectation is that more than 80% of patients admitted to CCUs will survive to hospital discharge. This reduced mortality trend also occurs in other patient groups where multi-organ failure are common and historical reports suggest poor survival rates, such as sepsis(12), poly-trauma, chronic obstructive airways disease(13) and haematological malignancy(14).

This increasing survival may relate to organisational improvements, protocols to reduce catheter-related bloodstream infections and ventilator associated pneumonia rates and training in critical care. Whether this

also occurs in patients with AD or ACLF is unknown. Liver-specific treatments such as liver-assist devices have not been shown to improve outcome(15), and use of liver transplantation for patients with cirrhosis and organ failure is rare. Prognostic pessimism has persisted on the benefit of organ support for patients with cirrhosis, especially outside LT centres (16). Nevertheless recent evidence from the USA suggests that survival for a hospital admission for decompensated cirrhosis is improving (17) although this study did not look at patients admitted ACLF.

Recent UK policy declarations reflect both the increasing numbers of patients with cirrhosis requiring treatment and potential deficiencies in care of patients with liver disease, particularly alcohol related liver disease (18, 19). It is not known whether the provision of critical care support is variable nationally in terms of numbers or patients admitted or in the resulting survival rates. It is an important moment to delineate the role of organ support in patients with cirrhosis given the recent re-evaluation of the care of these patients being undertaken(19). While outcomes for critically ill patients have improved markedly in recent decades, whether this is also the case for ACLF patients is less well defined outside specialist liver centres.

Here, we examine a large population of patients with cirrhosis requiring organ support in CCUs in England, Wales and Northern Ireland. Our aim was to describe the trends in outcome over time at a national level to guide clinical decision and policy making. We also compared the effect of alcohol as an aetiology on survival to hospital discharge and on whether readmission to critical care within the same hospital stay lead to similar survival rates.

METHODS

Case Mix Programme Database

The Case Mix Programme (CMP) is the national clinical audit for adult critical care in England, Wales and Northern Ireland. The Case Mix Programme Database (CMPD) contains pooled case mix, resource use and outcome data on consecutive admissions to participating units (both intensive care and combined intensive/high dependency units). Data are collected to precise rules and definitions, by trained data collectors, and undergo extensive local and central validation prior to pooling. Details of the data collection

and validation have been reported previously(20). The CMPD has been independently assessed to be of high quality(21) and support for the collection and use of patient-identifiable data without consent or need for institutional review board approval has been obtained under Section 251 of the NHS Act 2006 (approval number PIAG 2–10(f)/2005).

Selection of patients

Data were extracted for admissions to critical care between 1 January 1998 and 31 December 2012. Reason(s) for admission to critical care are coded using the ICNARC Coding Method (ICM), a hierarchical coding method specifically designed for coding reasons for admission to critical care(22). Cirrhosis cases were identified where primary, secondary or ultimate primary reason for admission were coded as variceal bleeding, alcoholic cirrhosis, acute alcoholic hepatitis, chronic cirrhosis (cause not defined) or portal hypertension, or where biopsy proven cirrhosis, portal hypertension or hepatic encephalopathy were reported in the past medical history (as per Acute Physiology And Chronic Health Evaluation (APACHE) II definitions(23)). The hierarchical method prevents patients with non-cirrhotic liver disease being included in this analysis.

Of the cirrhosis cases, four subgroups were identified. Alcohol related liver disease (ALRD) cases were identified where primary, secondary or ultimate primary reason for admission were either alcohol withdrawal seizures, alcoholic cirrhosis, acute alcoholic hepatitis, alcohol-induced chronic pancreatitis, self-poisoning with alcohol, alcohol overdose, delirium tremens or alcohol dependence and are compared to non-alcohol related cases. Haemorrhage cases were identified where primary, secondary or ultimate primary reason for admission were variceal bleeding and are compared to non-haemorrhage cases.

Cirrhosis cases were categorised into the following five geographical areas for analysis: South England, Midlands, North England, Wales and Northern Ireland

Case mix

Data were extracted for age, gender, ethnicity, deprivation, acute severity of illness, serum creatinine and blood lactate measurements. Liver function tests and liver specific prognostic score are not routinely captured in the CMP. Ethnicity was reported using the NHS ethnic codes, and categorized as White, Asian, Black and

Other ethnic group. Deprivation was assessed with the Index of Multiple Deprivation (IMD) 2010(24). Acute severity of illness was assessed with the ICNARC physiology score(25) [6], APACHE II Acute Physiology Score (APS) and APACHE II score(23). The ICNARC Physiology Score, APS and APACHE II score each encompass a weighting for acute physiology defined by derangement from the normal range for 12 physiological variables in the first 24 hours following admission to the critical care unit. The APACHE II score additionally encompasses a weighting for age and for severe conditions in the past medical history.

Outcome

Data were extracted for status at discharge from the CCU and status at discharge from acute hospital. Data on any readmissions to critical care within the same hospital stay were also extracted.

Analyses

Data were trended by year (1998 to 2012) or 5-year subgroups thereof. Case mix, outcomes and resource use, as defined above, were described per year for each of the following groups: all cirrhosis cases, ARLD and non-ARLD, haemorrhage cases and non-haemorrhage cases, as well as the five geographical subgroups. Categorical data were summarised as number and percentage; continuous data as mean (standard deviation, SD) or median (interquartile range, IQR).

Odds ratios for hospital mortality were calculated using multi-level logistic regression modelling, adjusting for age, gender, CPR prior to admission, location prior to admission, IMD quintile, ICNARC score, ARLD and year of admission with unit as a random effect.

A statistical analysis plan was agreed *a priori*. The analyses were performed using Stata 13 (Statacorp LP, TX, USA).

RESULTS

Incidence

31,363 patients with cirrhosis were identified in the study period out of 1,168,650 total admissions (2.7%). 558 patients out of a total 34,024 identified admissions (1.6%) in 1998 had cirrhosis rising to 4,207 out of 136,351 (3.1%) in 2012. Although coverage in the CMP did increase over this time, the extrapolated numbers show an increase from 1,450 out of 87,900 (1.6%) to 4750 out of 153,600 (3.1%). These admission rates are presented per 10000 population in Figure 1. The mean (SD) age of patients was 52.3 (12.7) years and 64.5% were male.

Mortality

The crude CCU mortality of patients with cirrhosis was 41.0 (95% CI 38.3-43.5) % in 1998-2002 falling to 32.5 (95% CI 30.6-33.8.1) % in 2008-2012. Crude hospital mortality was 57.4(95% CI 54.9-60.1) % in 1998-2002 and fell to 47.7 (95% CI 44.8-50.1) % in 2008-2012, see Table 1, Supplementary Material and Figures 1A and 1B. The analysis of geographical subgroups, index of deprivation and readmission is presented in the Supplementary Data.

Severity of illness at presentation

Mean (SD) APACHE II score in 1998-2002 was 20.6(8.3) and 19.6(7.3) in 2008-2012. The mean (SD) acute physiology component was 16.2(7.7) in 1998-2002 and 14.9 (6.6) in 2008-2012. The mean (SD) ICNARC score in 1998-2002 was 23.5(11.1) and 21.9 (10.2) in 2008-2012 (see per year in Table 2 and Figure 2). Mean (SD) highest serum creatinine for the cohort in 1998 was 176.9 (151.6) µmol/l and 148.0(136.7) µmol/l in 2012. Highest blood lactate was only available from 2008 where it was 4.5(4.4) mmol/l and 4.4 (4.2) mmol/l in 2012. The APACHE II risk of death for patients in 1998 was 47.6% and this was unchanged by 2012. Therefore, the observed mortality to expected risk of death discrepancy fell markedly during the study period.

Alcohol

10,936 patients were identified as having alcohol as the primary aetiological factor (35%). For patients with ARLD, crude hospital mortality fell from 66.7 (95% CI 58.9-73.6) % in 1998 to 58.1 (55.3-60.8) % in 2012. Crude CCU mortality fell from 50.9 (95% CI 43.3-58.5) % in 1998 to 41.9 (95% CI 39.3-44.6)% in 2012. Mean (SD) APACHE II score for patients with ARLD in 2012 was 20.6 (7.0) and 19.0 (7.2) for patients with a non-ARLD. Patients with ARLD had higher peak serum creatinine levels during the CCU stay (mean (SD) 161(150) µmol/l v 142(130) µmol/l for non-ARLD in 2012).

Resource use

For patients admitted from 2008 it was possible to capture the rates of patients undergoing advanced respiratory, renal or cardiovascular support. Advanced respiratory support was provided in 72.0% of cases in 2008 and 64.3% of cases in 2012. Advanced cardiovascular support was given in 42.7% of cases in 2008 falling to 27.6% in 2012. Renal support was given to 27.3% of patients in 2008 falling to 17.8% of patients in 2012. Mean CCU length of stay in 1998 was 3.8 (5.6) days and 5.7 (7.6) days in 2012, see Table 2.

In 2008 72.0% of patients with ARLD received advanced respiratory support while 67.4% did in 2012. Renal support was provided to 29.5% of patients with ARLD in 2008 and to 19.4% in 2012. There was a similar reduction in the number of cases receiving advanced cardiovascular support (45.8% in 2008 and 28.4% in 2012, see supplementary material).

Detailed data on liver assist devices was not possible within the ICNARC dataset but use of such devices (including MARS(26)) is not expected to have a significant impact on the outcome data described in this study (further details in Supplementary Material).

Multivariate analysis

Logistic regression analysis using hospital survival as the outcome variable and adjusting for age, sex, ICNARC score, year of admission, admission source location, index of deprivation, requirement for CPR prior to admission and alcohol as aetiology is shown in Table 3. This gave an odds ratio (OR) of 0.95 for year of admission (95% CI 0.94 to 0.96; $p<0.001$), showing a decrease in mortality over time after adjusting for

confounders. Alcohol as an aetiology for cirrhosis was associated with increased mortality (OR 1.51; 95% CI 1.42 to 1.61; p<0.001). The AUROC for the logistic regression model was 0.831 (95% CI 0.827 to 0.836), the Hosmer-Lemeshow $\chi 2$ statistic was 90 (8 df, p<0.001). Observed and predicted mortality were within +/-4% across the 10 categories.

DISCUSSION

These results demonstrate that patients with cirrhosis and organ failure have substantially improved survival in the modern era of critical care provision. Most patients admitted to critical care with cirrhosis in the UK are now expected to survive.

For decades the combination of a past medical history of cirrhosis and multi-organ failure has been perceived as having prohibitive mortality statistics and that organ support is futile(27). Survival to hospital discharge in patients with non-hepatic reasons for admissions have been increasing recently(12) due to a combination of factors including management of sepsis, attention to prevention of nosocomial infections (e.g. ventilator-associated pneumonia and catheter-related bloodstream infections) and organisation of CCUs. While individual factors are difficult to identify causally with decreasing mortality the background increasing survival rate is clear.

Tertiary liver centres with access to specialist hepatology, transplantation and hepatobiliary surgical expertise have demonstrated improved survival even when transplantation was discounted(11). The management of portal hypertensive bleeding especially has improved significantly. Several centres have reported decreasing mortality rates in patients with or without gastrointestinal haemorrhage as the primary indication for admission (10, 11). Both centres note a reduction in admission APACHE II score suggesting earlier admission to CCUs prior to irreversible MOF as a useful strategy. Furthermore, both transplant centres note that alcohol is not associated with a worse mortality compared to other aetiologies.

The data we present here demonstrate a different pattern. While mortality is falling, the acuity of critical illness on admission measured by APACHE II score (and predicted risk of death) did not change significantly. Admission ICNARC score fell by a small amount over the study period but after adjusting for this on multivariate analysis the year by year fall in mortality retained statistical significance. This suggests that while earlier admission is useful to manage impending organ failure, patients should not be denied admission based

on organ failure score alone and that the excess mortality associated with chronic liver disease (in addition to physiological APACHE score) is diminishing.

Our findings here confirm a more positive outlook for patients with cirrhosis and ACLF. While other authors have reported mortality rates of up to 80% in patients with ACLF-3 (3, 28) this was in the context of care outside of CCUs whereas all the patients in our study were cared for in CCUs. We would urge early admission to CCU to prevent irreversible organ failure occurring.

Overall this registry study represents the largest dataset of patients with cirrhosis managed in CCUs yet reported and therefore sets the benchmark of outcomes now expected in this patient group. It companions the epidemiological data in ALF(29) but for the first time demonstrates the improving outlook at population level for this important and more common subgroup of liver patients who require organ support.

While there may be country specific aspects in terms of interaction with liver transplantation services we expect these to impact the minority of patients given the access to LT in patients with ACLF has been limited in the past. This is because we exclude patients with ALF and transplantation is predominantly an elective procedure in patients with cirrhosis in most countries. Recent reports are challenging the dogma of whether LT is useful in patients with ACLF(30) which may lead to higher admission rates and greater access to LT services. As the UK moves to an organ allocation system based on wait list mortality it would be interesting to observe the impact on outcomes of patients after this change as those with organ failures will be more likely to receive an offer. In countries where MELD based allocation is already in use(31) it would be interesting to see if the outcomes of patients with cirrhosis and organ failure in general is different to what we report here.

In contrast to LT units we found that alcohol appears to be associated with an excess independent mortality risk even when confounders are addressed (although they tend to present with higher levels of organ (particularly renal) dysfunction). This discrepancy may be related to acute alcoholic hepatitis, which is associated with ongoing alcohol use and a high mortality. Our data would not allow clear delineation of this as retrospective allocation of diagnosis would require access to liver function tests, history of abstinence, imaging or liver biopsy data. We would not suggest that patients with ARLD be denied access to CCUs based on prohibitively high mortality until the underlying reason for this higher attributable mortality is identified. The number of patients receiving LT during the index admission in this dataset would be exceedingly small.

Doubt over appropriateness over the use of critical care services in actively drinking patients with ARLD may lead to delays in admission. Other investigators have noted an increased mortality in patients with ARLD who were consuming alcohol up to hospital admission (3). Of note we see a lower incidence of ALRD compared to other aetiologies in contrast to recent reports from the UK (1) which may be related to ARLD being defined from the reason for admission in the ICNARC dataset. This may represent under reporting or a reduced admission rate for ARLD outside LT centres.

This study has several limitations. We are unfortunately unable to calculate MELD, ACLF grade or CLIF-SOFA scores (or apply SOFA organ failure definitions) retrospectively from this data as the CMP was set up as a general CCU dataset with a strong focus on resource use. This is a weakness which does not allow prognostic scoring systems to be compared or validated in this otherwise very large cohort. The level of detail is sufficient to give guidance on the pattern of survival over time, corrected for general ICU severity measures, which is nevertheless still useful in overcoming prognostic pessimism about admission of patients with cirrhosis to CCUs.

We are unable to demonstrate definitively which patients were listed for LT following acute admission to the CCU for organ support. However, this is likely to be a small number compared to the overall cohort. It has been demonstrated previously in analysis of the UK national database of NHS Blood and Transplant that between 2011 to 2016 only 65 patients underwent LT following an acute hospitalisation with extra-hepatic organ failure(32). At present we are unable to demonstrate whether an unlisted patient was declined certain organ support modalities due to concerns over futility. This may occur for example in suspected HRS where bridging to LT was deemed futile. Further analysis will be required linking critical care and transplantation data sources to address these aspects in future studies.

The ICNARC dataset was not originally envisaged with liver disease as a primary aspect of study and so we are unable to give granular data beyond alcohol related liver disease in terms of aetiology. This limits the description of the major other aetiologies such as viral hepatitis or non-alcohol related fatty liver disease

(NAFLD) or rarer causes such as autoimmune hepatitis. In future NAFLD is likely to increase as a cause for cirrhosis and viral hepatitis will decrease rapidly given the effective treatments for hepatitis C. Future studies should focus on this aspect of the increasing burden of metabolic liver disease with more detailed aetiological descriptions.

We do not have information on long-term survival as although patients may survive the critical care or hospital stay their risk of death is still high and many will not survive the year following admission. However, these data provide further impetus for expedited transplant assessments in those patients who survive CCU admission.

In conclusion, the rising incidence of cirrhosis in the general population is reflected in increasing numbers of patients with cirrhosis admitted to CCUs. As critical care services expand it is vital that these patients are given access to organ support as the majority will survive to hospital discharge.

Figure Legends

Figure 1: (A) Extrapolated numbers of cirrhosis admissions and deaths per 100,000 of the population of England, Wales and Northern Ireland. (B) Acute hospital mortality of admissions to United Kingdom critical care units with cirrhosis

Figure 2: Physiology scores for cirrhosis admissions (APACHE II (Acute Physiology and Chronic Health Evaluation) and ICNARC (Intensive care national audit and research council) models, APS (acute physiology score).

Table Legends

Table 1: Demographics, outcome and critical care unit (CCU) and hospital length of stay (LOS). Years are grouped into 3 eras for ease of comparison, and in graphical form year by year in Figures 1 and 2. APS – acute physiology score, CI – confidence interval, IQR – interquartile range, SD – standard deviation.

Table 2: Resource use in this cohort in the final 5 years (where data were available). See Supplementary Material for definitions of the forms of support. Duration refers to median days of therapy received (IQR – interquartile range).

Table 3: Multivariate logistic regression for acute hospital mortality. The analysis includes year of critical care unit (CCU) admission and is adjusted for age, gender, cardiopulmonary resuscitation (CPR) prior to admission,

location prior to admission, alcohol related cirrhosis, index of multiple deprivation (IMD) quintile and Intensive Care National Audit and Research Centre (ICNARC) score, with random effects for unit* [N=28,449]

REFERENCES

1. Thomson SJ, Westlake S, Rahman TM, et al. Chronic liver disease--an increasing problem: a study of hospital admission and mortality rates in England, 1979-2005, with particular reference to alcoholic liver disease. Alcohol Alcohol 2008;43(4):416-422.
2. Roberts SE, Goldacre MJ, Yeates D. Trends in mortality after hospital admission for liver cirrhosis in an English population from 1968 to 1999. Gut 2005;54(11):1615-1621.
3. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology 2013;144(7):1426-1437, 1437 e1421-1429.
4. Shawcross DL, Austin MJ, Abeles RD, et al. The impact of organ dysfunction in cirrhosis: survival at a cost? J Hepatol 2012;56(5):1054-1062.
5. Aggarwal A, Ong JP, Younossi ZM, et al. Predictors of mortality and resource utilization in cirrhotic patients admitted to the medical ICU. Chest 2001;119(5):1489-1497.
6. Das V, Boelle PY, Galbois A, et al. Cirrhotic patients in the medical intensive care unit: early prognosis and long-term survival. Critical care medicine 2010;38(11):2108-2116.
7. Arabi Y, Ahmed QA, Haddad S, et al. Outcome predictors of cirrhosis patients admitted to the intensive care unit. Eur J Gastroenterol Hepatol 2004;16(3):333-339.
8. Cholongitas E, Senzolo M, Patch D, et al. Risk factors, sequential organ failure assessment and model for end-stage liver disease scores for predicting short term mortality in cirrhotic patients admitted to intensive care unit. Aliment Pharmacol Ther 2006;23(7):883-893.
9. Levesque E, Hoti E, Azoulay D, et al. Prospective evaluation of the prognostic scores for cirrhotic patients admitted to an intensive care unit. J Hepatol 2012;56(1):95-102.
10. Theocharidou E, Pieri G, Mohammad AO, et al. The Royal Free Hospital score: a calibrated prognostic model for patients with cirrhosis admitted to intensive care unit. Comparison with current models and CLIF-SOFA score. Am J Gastroenterol 2014;109(4):554-562.
11. McPhail MJ, Shawcross DL, Abeles RD, et al. Increased Survival for Patients With Cirrhosis and Organ Failure in Liver Intensive Care and Validation of the Chronic Liver Failure-Sequential Organ Failure Scoring System. Clin Gastroenterol Hepatol 2015;13(7):1353-1360 e1358.
12. Kaukonen KM, Bailey M, Suzuki S, et al. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. JAMA : the journal of the American Medical Association 2014;311(13):1308-1316.
13. Wildman MJ, Sanderson C, Groves J, et al. Implications of prognostic pessimism in patients with chronic obstructive pulmonary disease (COPD) or asthma admitted to intensive care in the UK within the COPD and asthma outcome study (CAOS): multicentre observational cohort study. Bmj 2007;335(7630):1132.
14. Bird GT, Farquhar-Smith P, Wigmore T, et al. Outcomes and prognostic factors in patients with haematological malignancy admitted to a specialist cancer intensive care unit: a 5 yr study. British journal of anaesthesia 2012;108(3):452-459.
15. Banares R, Catalina MV, Vaquero J. Molecular adsorbent recirculating system and bioartificial devices for liver failure. Clin Liver Dis 2014;18(4):945-956.
16. Berry PA, Thomson SJ, Rahman TM, et al. Review article: towards a considered and ethical approach to organ support in critically-ill patients with cirrhosis. Aliment Pharmacol Ther 2013;37(2):174-182.
17. Schmidt ML, Barritt AS, Orman ES, et al. Decreasing mortality among patients hospitalized with cirrhosis in the United States from 2002 through 2010. Gastroenterology 2015;148(5):967-977 e962.
18. Measuring the Units: A review of patients who died with alcohol-related liver disease. In: National Confidential Enquiry into Patient Outcome and Death; 2013.
19. Williams R, Aspinall R, Bellis M, et al. Addressing liver disease in the UK: a blueprint for attaining excellence in health care and reducing premature mortality from lifestyle issues of excess consumption of alcohol, obesity, and viral hepatitis. Lancet 2014;384(9958):1953-1997.
20. Harrison DA, Brady AR, Rowan K. Case mix, outcome and length of stay for admissions to adult, general critical care units in England, Wales and Northern Ireland: the Intensive Care National Audit & Research Centre Case Mix Programme Database. Crit Care 2004;8(2):R99-111.
21. Catalogue NI, Information Catalogue – Directory of Clinical Databases http://www.icapp.nhs.uk/docdat/. 2007.

22. Young JD, Goldfrad C, Rowan K. Development and testing of a hierarchical method to code the reason for admission to intensive care units: the ICNARC Coding Method. Intensive Care National Audit & Research Centre. British journal of anaesthesia 2001;87(4):543-548.
23. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Critical care medicine 1985;13(10):818-829.
24. Government DfCaL. English indices of deprivation. 2010.
25. Harrison DA, Parry GJ, Carpenter JR, et al. A new risk prediction model for critical care: the Intensive Care National Audit & Research Centre (ICNARC) model. Critical care medicine 2007;35(4):1091-1098.
26. Banares R, Nevens F, Larsen FS, et al. Extracorporeal albumin dialysis with the molecular adsorbent recirculating system in acute-on-chronic liver failure: the RELIEF trial. Hepatology 2013;57(3):1153-1162.
27. O'Brien AJ, Welch CA, Singer M, et al. Prevalence and outcome of cirrhosis patients admitted to UK intensive care: a comparison against dialysis-dependent chronic renal failure patients. Intensive care medicine 2012;38(6):991-1000.
28. Gustot T, Fernandez J, Garcia E, et al. Clinical Course of acute-on-chronic liver failure syndrome and effects on prognosis. Hepatology 2015;62(1):243-252.
29. Bernal W, Hyyrylainen A, Gera A, et al. Lessons from look-back in acute liver failure? A single centre experience of 3300 patients. J Hepatol 2013;59(1):74-80.
30. Artru F, Louvet A, Ruiz I, et al. Liver transplantation in the most severely ill cirrhotic patients: A multicenter study in acute-on-chronic liver failure grade 3. J Hepatol 2017;67(4):708-715.
31. Nekrasov V, Matsuoka L, Kaur N, et al. Improvement in the Outcomes of MELD >/= 40 Liver Transplantation: An Analysis of 207 Consecutive Transplants in a Highly Competitive DSA. Transplantation 2017;101(10):2360-2367.
32. Bernal W. Improving Outcomes for Transplantation of Critically Ill Patients with Cirrhosis? Clinical Liver Disease 2017;10(1):25-28.
33. Department of Health UK. The Critical Care Minimum Dataset. 2002.
34. Weil D, Levesque E, McPhail M, et al. Prognosis of cirrhotic patients admitted to intensive care unit: a meta-analysis. Annals of intensive care 2017;7(1):33.

Variable	1998-2002	2003-2007	2008-2012
Number of admissions with cirrhosis	4577	9698	17088
Total number of admissions	220784	378995	568871
Incidence of patients with cirrhosis/% (95% CI)	2.0 (1.9-2.1)	2.6(2.5-2.7)	3.0(2.9-3.1)
Males (%)	2793 (61)	5908 (61)	10580 (62)
Age / years (SD)	51.1 (12.4)	52.6(12.9)	53.2(12.3)
Alcohol-related N/ % (95% CI)	1571	3869	5496
	33 (28.8-37.3)	40 (38.8-41.5)	32 (31.0-33.7)
APACHE II Score (SD)	20.6(8.3)	20.3(8.1)	19.6(7.3)
APACHE II APS (SD)	16.2(7.7)	16.1(7.4)	14.9(6.6)
ICNARC Score (SD)	23.5(11.5)	23.1(11)	21.9(10.1)
CCU LOS / days (IQR)	2.1 (0.8-5.5)	2.4 (1.0-6.3)	2.6(1.2-6.8)
Survivors	2.0 (0.9-5.0)	2.6 (1.2-6.4)	3.0(1.5-6.8)
Non-survivors	2.1 (0.8-6.2)	2.1 (0.8-6.2)	2.4 (0.8-6.7)
Hospital LOS / days (IQR)	14(8-25)	16(8-28)	15 (6-27)
Survivors	22 (13-41)	22 (12-40)	19 (10-36)
Non-survivors	8 (3-18)	9 (3-19)	9 (3-20)
CCU Mortality/% (95%CI)	41.0 (38.3-43.5)	37.8 (35.6-41.9)	32.5(30.6-33.8)
Hospital Mortality/% (95%CI)	57.4(54.9-60.1)	55.4(52.9-57.3)	47.7(44.8-50.1)

Table 1: Demographics, outcome and critical care unit (CCU) and hospital length of stay (LOS). Years are grouped into 3 eras for ease of comparison, and in graphical form year by year in Figures 1 and 2. APS – acute physiology score, CI – confidence interval, IQR – interquartile range, SD – standard deviation.

Variable	2008	2009	2010	2011	2012
Advanced respiratory support					
Number, n (%)	1,849 (72.0)	2,022 (69.1)	2,342 (68.2)	2,589 (65.5)	2,706 (64.3)
Duration / days (IQR)	3 (2-7)	3 (2-8)	3 (2-7)	3 (2-7)	3 (2-7)
Basic cardiovascular support					
Number, n (%)	2,199 (85.6)	2,522 (86.2)	2,947 (85.9)	3,440 (87.0)	3,694 (87.8)
Duration / days (IQR)	3 (2-6)	4 (2-7)	3 (2-7)	3 (2-6)	3 (2-7)
Advanced cardiovascular support					
Number, n (%)	1,098 (42.7)	986 (33.7)	1,064 (31.0)	1,216 (30.8)	1,161 (27.6)
Duration / days (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	2 (-,3)	2 (1-4)
Renal support					
Number, n (%)	702 (27.3)	580 (19.8)	614 (17.9)	735 (18.6)	747 (17.8)
Duration median (IQR)	3 (2-6)	3 (2-6)	4 (2-8)	3 (2-6)	3 (2-6)

Table 2: Resource use in this cohort in the final 5 years (where data were available). See Supplementary Material for definitions of the forms of support. Duration refers to median days of therapy received (IQR – interquartile range).

Variable	Odds ratio (95% confidence interval)	p value
Age	1.02 (1.02,1.03)	<0.001
Gender (male)	1.01 (0.95,1.07)	0.71
CPR prior to admission	1.87 (1.61,2.18)	<0.001
Location prior to admission		
A&E/Other/Not in hospital	1.00 (-)	-
ICU/HDU	1.26 (1.12,1.41)	<0.001
Theatre (elective)	0.38 (0.32,0.44)	<0.001
Theatre (emergency)	0.81 (0.73,0.89)	<0.001
Ward	1.64 (1.52,1.77)	<0.001
Alcohol related cirrhosis	1.51 (1.42,1.61)	<0.001
IMD quintile		
1 (least deprived)	1.00 (-)	-
2	1.02 (0.91,1.14)	0.70
3	1.06 (0.95,1.18)	0.30
4	1.08 (0.97,1.20)	0.16
5 (most deprived)	1.07 (0.97,1.19)	0.16
ICNARC score	1.13 (1.13,1.14)	<0.001
Year of ICU admission	0.95 (0.94,0.96)	<0.001

***rho=0.02 (0.02,0.03)**

Table 3: Multivariate logistic regression for acute hospital mortality. The analysis includes year of critical care unit (CCU) admission and is adjusted for age, gender, cardiopulmonary resuscitation (CPR) prior to admission, location prior to admission, alcohol related cirrhosis, index of multiple deprivation (IMD) quintile and Intensive Care National Audit and Research Centre (ICNARC) score, with random effects for unit* [N=28,449]

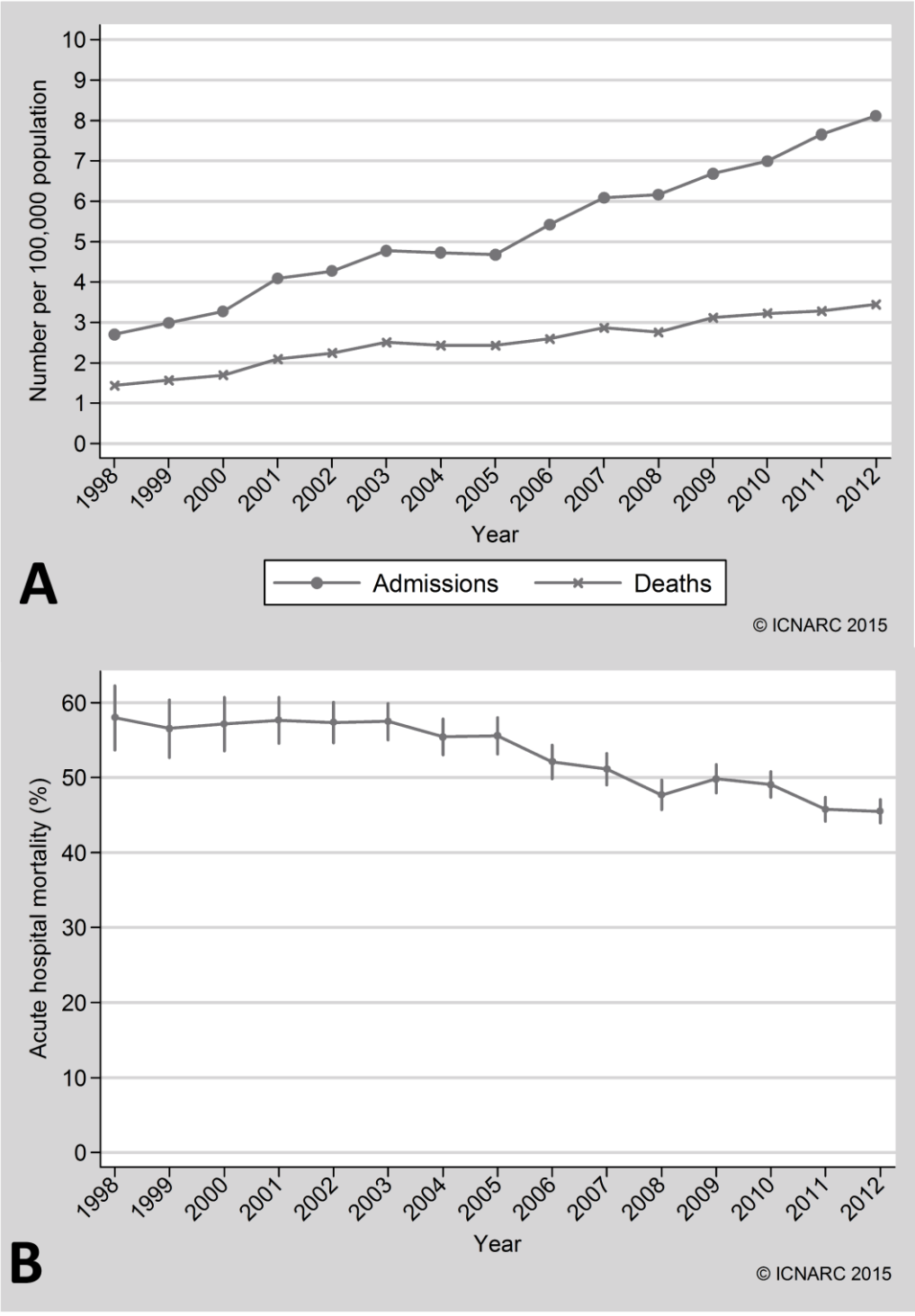

Figure 1: (A) Extrapolated numbers of cirrhosis admissions and deaths per 100,000 of the population of England, Wales and Northern Ireland. (B) Acute hospital mortality of admissions to United Kingdom critical care units with cirrhosis

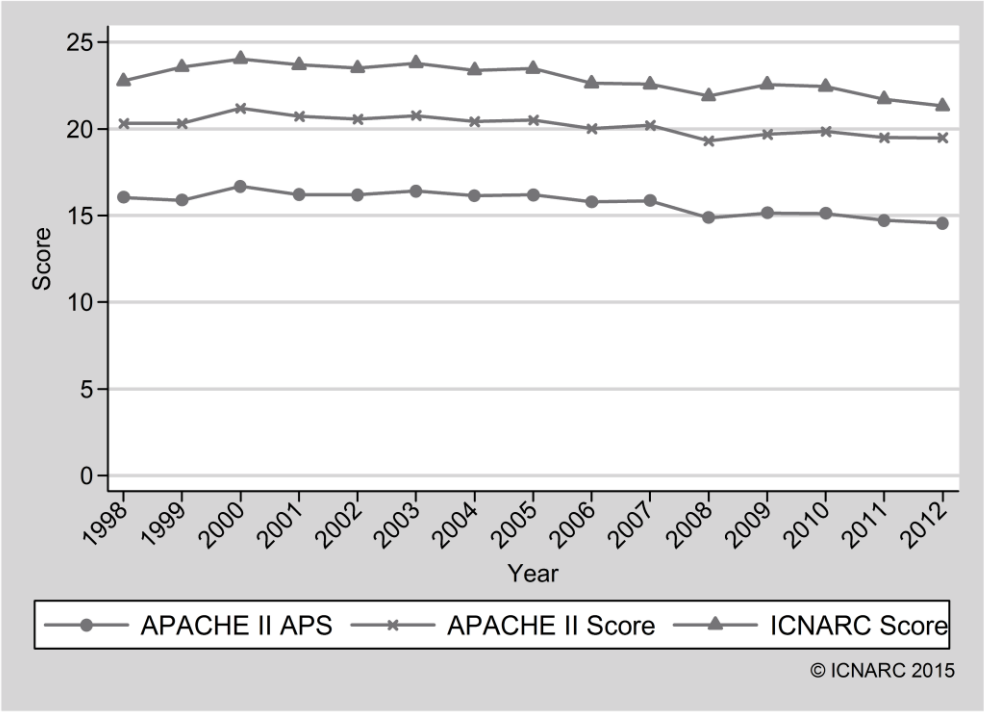

Figure 2: Physiology scores for cirrhosis admissions (APACHE II (Acute Physiology and Chronic Health Evaluation) and ICNARC (Intensive care national audit and research council) models, APS (acute physiology score).

Supplementary Material

Supplementary Methods

Resource use

Data were extracted for type and duration of organ support, length of stay in the critical care unit and length of stay in acute hospital. Duration of organ support was measured in calendar days (00:00 to 23:59 or part thereof) at any point during the critical care unit stay for advanced respiratory, basic cardiovascular, advanced cardiovascular and renal, defined as per the Department of Health Critical Care Minimum Data Set (CCMDS)(33) and defined below. Critical care unit length of stay was the duration in days from the date and time of admission to the critical care unit to discharge from, or death in, the critical care unit. The total acute hospital length of stay was the duration in days from the date of original admission to an acute hospital to the date of ultimate discharge from, or death in, an acute hospital.

Due to increasing coverage of the CMP over the study period, extrapolation was used to estimate absolute numbers for the whole of England, Wales and Northern Ireland. The number of admissions with cirrhosis was extrapolated by calculating the actual number of critical care admissions, per year, for each unit, averaging over all units, and multiplying by the total number of units in England, Wales and Northern Ireland. The number of critical care unit admissions with cirrhosis was also extrapolated within each of the geographical subgroups. Extrapolated numbers of critical care unit deaths and acute hospital deaths per year were also estimated for all cirrhosis cases and for the five geographical subgroups.

The number of admissions with cirrhosis and the number of deaths following admission to CCU for cirrhosis were extrapolated to provide a rate per 100,000 of the population of England, Wales and Northern Ireland (using the mid-year population estimates from the Office for National Statistics).

As per STROBE guidelines p-values were not generated for longitudinally trended data although confidence intervals were calculated.

The index of multiple deprivation is a UK government statistic based on qualitative data from local councils (administrative areas). It is based on statistics derived from 7 areas of social and economic activity associated with deprivation namely – Income, Employment, Health Deprivation and Disability, Education Skills and Training, Barriers to Housing and Services, Crime, Living Environment. It was originally developed at the Social Disadvantage Research Centre, Oxford University. Each domain has a number of indicators totalling 37. It has

been updated several times and is based on small areas defined by the UK Census in 2001 as super output areas (SOA) and the smaller areas of the updated index uses a minimum of 400 households and 1000 people.

CCMDS definitions

Basic cardiovascular support

Use of a central venous catheter (CVC) for basic monitoring of CVP pressure and/or for the use of delivering drugs or fluid challenges to treat hypovolaemia
Use of an arterial line for basic monitoring of arterial blood pressure or for obtaining blood samples for analysis.
Administration of a single intravenous vasoactive drug (regardless of dose) used to support low arterial blood pressure, cardiac output or organ perfusion or control high blood pressure
Intravenous drugs to control cardiac arrhythmias

Advanced cardiovascular support

Multiple intravenous vasoactive and/or rhythm controlling drugs used simultaneously to support arterial blood pressure, cardiac output or organ perfusion (eg vasopressors, inotropes, chronotropes, nitrates)
Observation of cardiac output and derived Indices (eg PA catheter, lithium dilution, pulse contour analysis, oesophageal Doppler)
Insertion and/or continuing use of a temporary trans-venous cardiac Pacemaker
Intra-aortic balloon pump support

Advanced respiratory support

ECMO, IVOX (Extra corporeal respiratory support)
Invasive mechanical ventilatory support (i.e: IPPV or BIPAP) Via Endotracheal tube (ETT)
BIPAP pressure support ventilation via ETT/Trachy
CPAP via ETT
Patients remaining intubated (>12 hours) post operatively pending respiratory, cardiovascular, other instability being resolved (to support specific end organ protection)

Renal support

Acute renal replacement therapy (eg haemofiltration)
Patients receiving haemofiltration for chronic renal failure and requiring other organ support within critical care

Supplementary Results

Haemorrhage

The ability to code for cases admitted primarily for the management of gastrointestinal haemorrhage (GIH) was only available from 2002. In that year 3.7 (2.8-4.8) % of cases were attributable to GIH and in 2012 this was 2.3 (1.9-2.8) %. Crude critical care unit mortality in the GIH cases was 36.5 (24.8-50.1) % in 2002 and 33.0(24.4-42.8) % in 2012. Crude hospital mortality in the GIH cases was 54.0(40.4-67.0) % in 2002 and 54.4 (44.2-64.3) % in 2012. Because of the shorter longitudinal cohort and small number of cases GIH was not carried forward as a factor into multivariate analysis and these results should be viewed with caution.

Readmissions

Survival data for patients readmitted to critical care during the same hospital stay was available from 2006. In 2006 131 patients were readmitted out of 1088 (12.0%) admissions discharged to a location within the same

hospital and in 2012 231 out of 2434 (9.5%) were readmitted. Crude hospital mortality for readmissions was 31.1% in 2006 and 32.1% in 2012. This compares favourably with the hospital mortality of the entire cohort (see Supplementary Tables).

Index of deprivation

More admissions were seen for patients from lower IMD areas. In 2012 (representative of entire cohort) 489/4165 (11.7%) patients were from IMD 1, 602 (14.5%) from IMD 2, 759 (18.2) from IMD 3, 965 (23.2%) from IMD 4 and 1350(32.4%) from IMD 5 areas. This was reflected in earlier years. There was no significant difference in this pattern for patients with or without alcohol as an aetiology.

Regional variations

Crude acute hospital mortality appeared higher in Wales (50.5 (95% CI 43.7-57.2) % in 2012) and Northern Ireland (58.1 (49.1-66.7) % in 2012) compared to English regions (South 45.3 (42.7-47.8) %, Midlands 42.1 (38.8-45.4) %, North 46.0(43.4-48.8) % in 2012). The pattern of improvement in survival over the study period was maintained throughout the regions studied in the data available from 2001. Of note the number of admissions to the Welsh or Northern Irish regions was often 100 patients or less per year. For this reason, area of the United Kingdom was not used as a factor in multivariate analysis.

Liver assist devices

Molecular Adsorbent Recirculating System (MARS) was initially used as part of several research studies into liver assist devices in patients with a number of liver failure syndromes including alcoholic hepatitis and ACLF. Those with cirrhosis and ACLF would be relevant here but the number of units and patients undergoing MARS for this indication was very low in the UK. As part of the RELIEF study UK units randomised patients to MARS or SMT and of a total of 95 patients across Europe < 10 in the UK would have received MARS(26). RELIEF was negative in terms of outcome benefit and therefore is unlikely to have impacted our results. Data from our recent meta-analysis on the outcome of patients with cirrhosis in ICU is also instructive. MARS use was noted in 1485 patients worldwide(34) and is associated with a worse outcome (compared to those who did not

receive it rather than in an RCT) and the authors do not recommend MARS in patients with ACLF. Further studies in other modalities of liver assist are awaited.

Within ICNARC liver support is defined as "admissions receiving management of coagulopathy and/or management of portal hypertension (including liver purification and detoxification techniques) for either: acute on chronic hepatocellular failure; or primary acute hepatocellular failure whilst being considered for transplantation." Therefore, this is broader than the *de facto* hepatological definition of using a specific physical device to provide liver support. This is the reason that in 2012 the ICNARC defined liver support numbers reached 734 per year (independent of alcohol as the primary aetiology), suggesting this is capturing more medical supportive strategies. Further granularity on this aspect will be addressed in future studies.

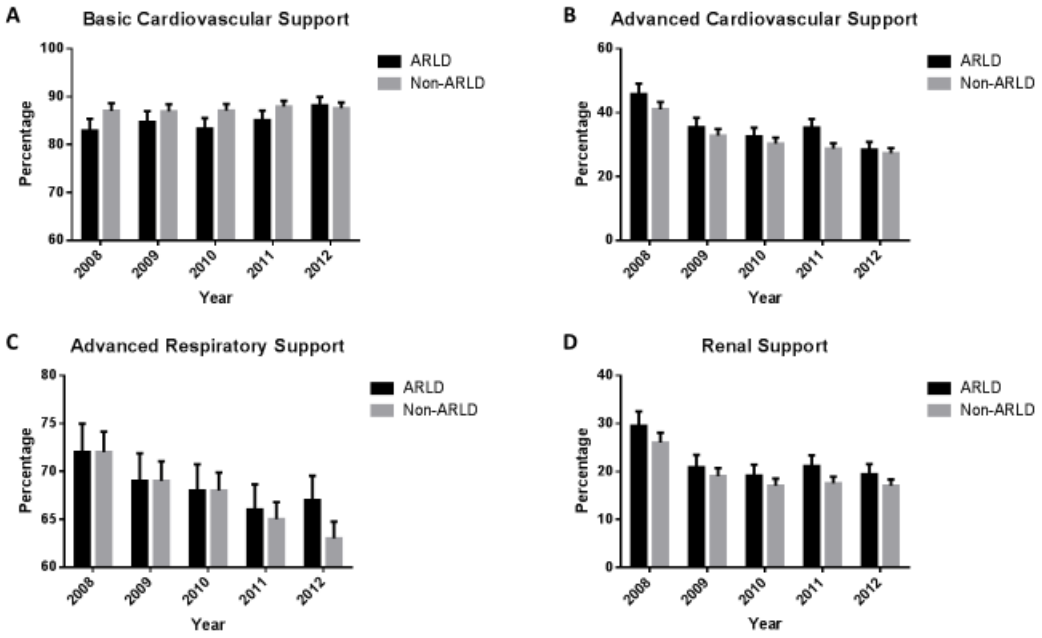

Figure S1: Organ support resource use from 2008 to 2012 showing the percentage of patients with alcohol related liver disease (ARLD) or non ARLD who received cardiovascular, respiratory or renal support (error bars 95% CI of the proportion).

Supplementary Discussion

At present, we were not able to meaningfully compare survival rates for patients admitted with or without haemorrhage as a primary indication for admission or by geographical area due to small numbers. Transplant centres have reported improved survival for patients with variceal haemorrhage as an indication to admit based on early airway control to prevent aspiration and modern methods to treat bleeding. Transplant centres may be more likely to admit patients to critical care compared to general units where haemostasis may be achieved in operating rooms without use of the critical care unit. In the case of geographical variation while

Wales and Northern Ireland appear to have higher mortality rates for patients with cirrhosis admitted to critical care the numbers are small compared to the four main English regions. Whether this represents reduced incidence in the general population, reluctance to admit patients or differences in management is unknown at this stage but warrants further investigation as areas with higher numbers of admission (or easier access to transplant centres) may have higher survival rates through better experience in managing such cases.

Although survival rates are increasing the proportion of patients receiving advanced organ (particularly cardiovascular and renal) support appears to be falling which cannot be explained by the small shift in organ failure scores. There may be reluctance to provide all modalities of organ support and a limitation imposed on the use of e.g. renal replacement therapy due to perceived futility in hepato-renal syndrome. In our previously reported cohort with a slightly higher APACHE II score profile over 40% of patients received RRT and the majority underwent mechanical ventilation(11). CCU survival was 55% and hospital survival 48% with a marked improvement in later years (APACHE II adjusted OR 0.89 (95%CI 0.86-0.95)/ year) suggesting there may be a benefit in early and initially unlimited organ support.

Further data is provided below on physiology scores, regional variations in outcome and organ support and on alcohol and haemorrhage as the main indication for intensive care unit admission.

Supplementary Tables

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Number of admissions, n (%) {CI} [N]	558 (1.6) {1.5,1.8} [34,024]	689 (1.8) {1.7,1.9} [38,566]	802 (2.0) {1.9,2.1} [40,415]	1,109 (2.3) {2.2,2.5} [47,806]	1,419 (2.4) {2.2,2.5} [59,973]	1,754 (2.5) {2.4,2.6} [69,904]	1,780 (2.4) {2.3,2.5} [74,181]	1,750 (2.3) {2.2,2.4} [75,124]	2,058 (2.7) {2.6,2.8} [76,670]	2,356 (2.8) {2.7,2.9} [83,116]	2,569 (2.8) {2.7,2.9} [92,107]	2,927 (3.0) {2.9,3.1} [97,547]	3,432 (3.0) {2.9,3.1} [114,207]	3,953 (3.1) {3.0,3.2} [128,659]	4,207 (3.1) {3.0,3.2} [136,351]
Age, mean (SD)	50.1 (13.5)	51.0 (13.5)	51.3 (12.5)	51.1 (12.4)	52.0 (12.8)	52.6 (12.7)	52.5 (12.9)	53.1 (12.6)	51.9 (12.7)	52.8 (12.9)	53.2 (12.8)	52.7 (12.5)	53.5 (12.3)	53.1 (12.3)	53.5 (12.7)
Number of males, n (%)	315 (56.5)	421 (61.1)	514 (64.1)	688 (62.0)	855 (60.3)	1,088 (62.0)	1,073 (60.3)	1,084 (61.9)	1,238 (60.2)	1,425 (60.5)	1,597 (62.2)	1,804 (61.6)	2,109 (61.5)	2,415 (61.1)	2,655 (63.1)
Ethnicity, n (%)															
White											1,979 (89.2)	2,621 (89.6)	3,157 (92.4)	3,573 (91.4)	3,829 (91.5)
Asian											104 (4.7)	130 (4.4)	123 (3.6)	162 (4.1)	169 (4.0)
Black											23 (1.0)	43 (1.5)	41 (1.2)	53 (1.4)	57 (1.4)
Other											23 (1.0)	37 (1.3)	41 (1.2)	53 (1.4)	61 (1.5)
Not stated											90 (4.1)	94 (3.2)	53 (1.6)	67 (1.7)	67 (1.6)
Deprivation IMD quintile, n (%)															
1 (least deprived)	58 (11.0)	74 (11.3)	99 (12.8)	137 (12.7)	170 (12.4)	220 (12.9)	200 (11.4)	211 (12.2)	255 (12.6)	287 (12.3)	324 (12.8)	368 (12.7)	422 (12.4)	491 (12.5)	489 (11.7)
2	86 (16.3)	109 (16.6)	106 (13.7)	142 (13.2)	199 (14.6)	254 (14.8)	282 (16.1)	234 (13.6)	302 (14.9)	419 (17.9)	392 (15.5)	471 (16.2)	517 (15.2)	555 (14.2)	602 (14.5)
3	94 (17.9)	115 (17.6)	139 (18.0)	206 (19.2)	239 (17.5)	310 (18.1)	288 (16.4)	326 (18.9)	314 (15.5)	386 (16.5)	476 (18.8)	484 (16.7)	620 (18.3)	719 (18.3)	759 (18.2)
4	111 (21.1)	134 (20.5)	155 (20.1)	232 (21.6)	286 (20.9)	341 (19.9)	356 (20.3)	358 (20.7)	452 (22.3)	496 (21.2)	566 (22.3)	602 (20.8)	726 (21.4)	904 (23.1)	965 (23.2)
5 (most deprived)	177 (33.7)	223 (34.0)	272 (35.3)	358 (33.3)	473 (34.6)	587 (34.3)	626 (35.7)	597 (34.6)	706 (34.8)	749 (32.0)	777 (30.7)	974 (33.6)	1,106 (32.6)	1,251 (31.9)	1,350 (32.4)
CPR prior to admission, n (%)	45 (8.1)	51 (7.4)	69 (8.6)	80 (7.2)	104 (7.3)	97 (5.5)	110 (6.2)	127 (7.3)	112 (5.4)	108 (4.6)	114 (4.4)	157 (5.4)	190 (5.5)	201 (5.1)	199 (4.7)
Highest serum creatinine*, mean (SD)	176.9 (151.6)	168.3 (135.1)	162.1 (124.5)	167.3 (143.7)	164.1 (137.9)	171.4 (147.3)	161.7 (137.0)	161.1 (133.4)	159.0 (143.7)	157.0 (128.8)	155.7 (139.3)	165.7 (149.9)	158.3 (138.6)	153.6 (143.8)	148.0 (136.7)
Highest blood lactate, mean (SD)**											4.5 (4.4)	4.6 (4.4)	4.7 (4.3)	4.5 (4.4)	4.4 (4.2)
Location immediately prior to admission, n (%)															
A&E/other/not in hospital	89 (15.9)	102 (14.9)	128 (16.0)	192 (17.3)	264 (18.6)	284 (16.2)	328 (18.4)	285 (16.3)	399 (19.4)	491 (20.8)	560 (21.8)	594 (20.3)	725 (21.1)	825 (20.9)	903 (21.4)

Critical care	55 (9.9)	71 (10.3)	84 (10.5)	146 (13.2)	170 (12.0)	219 (12.5)	217 (12.2)	182 (10.4)	220 (10.7)	219 (9.3)	263 (10.2)	262 (9.0)	341 (9.9)	324 (8.2)	302 (7.2)
Theatre (elective)	77 (13.8)	74 (10.8)	79 (9.9)	95 (8.6)	171 (12.1)	179 (10.2)	193 (10.9)	157 (9.0)	159 (7.7)	214 (9.1)	199 (7.8)	218 (7.5)	250 (7.3)	286 (7.2)	321 (7.6)
Theatre (emergency)	88 (15.8)	142 (20.7)	179 (22.4)	203 (18.3)	218 (15.4)	257 (14.7)	261 (14.7)	261 (14.9)	371 (18.1)	370 (15.7)	447 (17.4)	541 (18.5)	565 (16.5)	686 (17.4)	778 (18.5)
Ward	249 (44.6)	297 (43.3)	330 (41.3)	471 (42.5)	595 (42.0)	814 (46.4)	779 (43.8)	865 (49.4)	906 (44.1)	1,061 (45.1)	1,098 (42.8)	1,311 (44.8)	1,551 (45.2)	1,831 (46.3)	1,906 (45.3)

*Missing data for 26% of admissions
**Missing data for 13% of admissions

Table S1: Demographics and case mix of this cohort of patients with cirrhosis admitted to United Kingdom critical care units participating in the case mix programme including further data not included in Table 1 in the main document.

	1998	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**
Critical care unit mortality, deaths (%) {CI} [N]	227 (40.7) {36.7,44.8} [558]	290 (42.1) {38.5,45.8} [689]	343 (42.8) {39.4,46.2} [802]	449 (40.5) {37.6,43.4} [1,109]	570 (40.2) {37.6,42.7} [1,419]	712 (40.6) {38.3,42.9} [1,754]	691 (38.8) {36.6,41.1} [1,780]	681 (38.9) {36.7,41.2} [1,750]	744 (36.2) {34.1,38.3} [2,058]	838 (35.6) {33.7,37.5} [2,356]	859 (33.4) {31.6,35.3} [2,569]	1,027 (35.1) {33.4,36.8} [2,927]	1,138 (33.2) {31.6,34.8} [3,432]	1,217 (30.8) {29.4,32.2} [3,953]	1,291 (30.7) {29.3,32.1} [4,207]
Acute hospital mortality, deaths* (%) {CI} [N]	297 (58.0) {53.7,62.2} [512]	362 (56.6) {52.7,60.4} [640]	415 (57.2) {53.5,60.7} [726]	568 (57.7) {54.6,60.7} [985]	744 (57.4) {54.7,60.0} [1,297]	920 (57.5) {55.1,59.9} [1,600]	914 (55.4) {53.0,57.8} [1,649]	910 (55.6) {53.2,58.0} [1,637]	984 (52.1) {49.8,54.3} [1,889]	1,109 (51.1) {49.0,53.2} [2,169]	1,149 (47.7) {45.7,49.7} [2,410]	1,363 (49.8) {48.0,51.7} [2,735]	1,580 (49.1) {47.3,50.8} [3,220]	1,695 (45.8) {44.2,47.4} [3,704]	1,787 (45.5) {43.9,47.1} [3,928]
Number of patients readmitted, n (%) [N]**	32 (12.6) [254]	35 (10.7) [328]	50 (13.8) [362]	87 (16.8) [519]	93 (13.1) [709]	110 (12.8) [860]	104 (11.2) [929]	84 (9.3) [900]	131 (12.0) [1,088]	139 (11.0) [1,258]	123 (8.6) [1,431]	146 (9.2) [1,581]	179 (9.4) [1,907]	222 (9.8) [2,271]	231 (9.5) [2,434]

Acute hospital mortality of patients who are readmitted, deaths (%) [N]	61 (31.1) [126]	62 (29.4) [134]	59 (31.6) [123]	79 (37.3) [145]	88 (32.7) [178]	91 (25.9) [221]	112 (32.1) [230]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S2: Critical care and hospital mortality including patients readmitted during the same hospital stay (from 2006 onwards) of this cohort of patients with cirrhosis admitted to United Kingdom critical care units participating in the case mix programme.

Table S3a: Geographical area (South) – Demographics and case mix

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Number of admissions, n (%) {CI} [N]	297 (2.3) {2.0,2.5} [13,192]	420 (2.3) {2.1,2.5} [18,113]	511 (2.4) {2.2,2.6} [21,233]	497 (2.2) {2.0,2.4} [22,482]	544 (2.3) {2.2,2.5} [23,281]	685 (2.9) {2.7,3.1} [23,934]	812 (2.9) {2.7,3.1} [27,747]	920 (2.8) {2.6,3.0} [32,660]	935 (2.9) {2.7,3.1} [32,579]	1,204 (3.0) {2.8,3.2} [40,385]	1,400 (2.9) {2.8,3.1} [47,710]	1,548 (3.1) {2.9,3.3} [50,016]
Extrapolated number of admissions, n (%) [N]	1,050 (2.3) [46,000]	1,100 (2.3) [46,700]	1,100 (2.4) [46,100]	1,050 (2.2) [47,200]	1,100 (2.3) [48,000]	1,350 (2.9) [46,950]	1,550 (2.9) [53,350]	1,450 (2.8) [52,150]	1,500 (2.9) [51,650]	1,650 (3.0) [55,200]	1,750 (2.9) [59,800]	1,900 (3.1) [61,800]
Age, mean (SD)	51.4 (13.5)	51.9 (12.5)	52.6 (12.1)	52.5 (12.8)	54.5 (11.7)	52.2 (12.8)	53.3 (12.7)	53.3 (12.4)	53.3 (12.2)	54.9 (12.1)	54.1 (12.1)	54.4 (12.3)
Number of males, n (%)	170 (57.2)	276 (65.7)	344 (67.3)	311 (62.6)	343 (63.1)	429 (62.6)	525 (64.7)	587 (63.8)	581 (62.1)	766 (63.6)	858 (61.3)	993 (64.1)
Ethnicity , n (%)												
White								686 (85.3)	771 (82.5)	1,050 (88.5)	1,180 (87.1)	1,330 (87.3)
Asian								49 (6.1)	59 (6.3)	64 (5.4)	69 (5.1)	80 (5.2)
Black								17 (2.1)	30 (3.2)	28 (2.4)	42 (3.1)	44 (2.9)
Other								14 (1.7)	14 (1.5)	22 (1.9)	31 (2.3)	30 (2.0)
Not stated								38 (4.7)	61 (6.5)	23 (1.9)	33 (2.4)	40 (2.6)
Deprivation IMD quintile , n (%)												
1 (least deprived)	43 (15.0)	44 (11.1)	62 (12.5)	57 (11.7)	68 (12.7)	100 (14.9)	115 (14.3)	133 (14.8)	152 (16.5)	177 (15.0)	196 (14.2)	197 (12.8)
2	50 (17.4)	66 (16.7)	70 (14.1)	70 (14.4)	74 (13.9)	103 (15.4)	171 (21.3)	152 (16.9)	167 (18.1)	191 (16.2)	229 (16.6)	203 (13.2)
3	64 (22.3)	77 (19.5)	111 (22.3)	92 (18.9)	123 (23.0)	115 (17.2)	140 (17.5)	191 (21.2)	169 (18.3)	237 (20.1)	284 (20.5)	317 (20.7)
4	70 (24.4)	86 (21.8)	115 (23.1)	128 (26.3)	117 (21.9)	179 (26.7)	189 (23.6)	213 (23.7)	223 (24.2)	308 (26.2)	373 (27.0)	422 (27.5)
5 (most deprived)	60 (20.9)	122 (30.9)	139 (28.0)	139 (28.6)	152 (28.5)	173 (25.8)	187 (23.3)	211 (23.4)	211 (22.9)	264 (22.4)	300 (21.7)	395 (25.7)
APACHE II Acute Physiology Score, mean (SD)	16.9 (7.2)	16.4 (6.9)	16.7 (7.4)	15.8 (6.9)	16.6 (7.0)	15.8 (7.1)	15.9 (7.1)	14.8 (6.7)	15.2 (6.8)	15.3 (6.6)	14.5 (6.2)	14.4 (6.3)
APACHE II score, mean (SD)	21.4 (8.1)	20.7 (7.5)	21.0 (7.9)	20.1 (7.4)	21.2 (7.7)	20.5 (7.9)	20.4 (7.7)	19.4 (7.4)	20.1 (7.5)	20.5 (7.2)	19.6 (6.9)	19.7 (6.9)
ICNARC physiology score, mean (SD)	24.3 (10.6)	23.7 (10.9)	23.9 (11.3)	23.0 (11.1)	24.2 (10.5)	22.5 (10.5)	22.3 (10.3)	21.8 (9.8)	23.0 (10.4)	22.9 (10.1)	21.4 (9.8)	21.6 (10.4)
Highest serum creatinine*, mean (SD)	168.8 (174.8)	155.4 (129.5)	162.5 (124.7)	149.1 (122.0)	156.6 (126.6)	156.6 (162.8)	154.7 (127.5)	152.8 (136.9)	167.0 (143.6)	159.2 (144.6)	154.3 (145.1)	146.3 (133.5)
Highest blood lactate, mean (SD)**								4.5 (4.5)	4.6 (4.3)	4.6 (4.2)	4.5 (4.3)	4.5 (4.2)

*Missing data for 24% of admissions

**Missing data for 12% of admissions

Table S3b: Geographical area (South) – Outcomes

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Critical care unit mortality, deaths (%) {CI} [N]	125 (42.1) {36.6,47.8} [297]	173 (41.2) {36.6,46.0} [420]	227 (44.4) {40.2,48.8} [511]	203 (40.8) {36.6,45.2} [497]	235 (43.2) {39.1,47.4} [544]	242 (35.3) {31.8,39.0} [685]	299 (36.8) {33.6,40.2} [812]	292 (31.7) {28.8,34.8} [920]	324 (34.7) {31.7,37.8} [935]	423 (35.1) {32.5,37.9} [1,204]	438 (31.3) {28.9,33.8} [1,400]	466 (30.1) {27.9,32.4} [1,548]
Acute hospital mortality*, deaths (%) {CI} [N]	172 (63.7) {57.8,69.2} [270]	228 (60.2) {55.2,65.0} [379]	295 (63.3) {58.8,67.6} [466]	270 (58.2) {53.7,62.6} [464]	310 (60.8) {56.5,64.9} [510]	314 (52.0) {48.0,55.9} [604]	404 (53.9) {50.4,57.5} [749]	391 (44.9) {41.6,48.2} [871]	445 (51.0) {47.7,54.3} [873]	592 (51.9) {49.0,54.8} [1,141]	628 (47.7) {45.0,50.4} [1,317]	655 (45.3) {42.7,47.8} [1,447]
Extrapolated acute hospital mortality, deaths (%) [N]	600 (63.7) [950]	600 (60.2) [1,000]	650 (63.3) [1,000]	550 (58.2) [950]	650 (60.8) [1,050]	600 (52.0) [1,200]	800 (53.9) [1,450]	600 (44.9) [1,400]	700 (51.0) [1,400]	800 (51.9) [1,550]	800 (47.7) [1,650]	800 (45.3) [1,800]
Number of patients readmitted, n (%) [N]**	27 (20.6) [131]	33 (16.4) [201]	33 (14.4) [229]	27 (10.6) [255]	25 (9.7) [259]	58 (16.3) [356]	50 (12.2) [411]	33 (6.2) [529]	47 (9.5) [494]	54 (8.5) [638]	74 (9.4) [784]	92 (10.3) [891]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S3c: Geographical area (South) – Resource use

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support												
Number, n (%)								644 (70.0)	646 (69.1)	805 (66.9)	915 (65.4)	976 (63.0)
Duration (All), median (IQR)								2 (0,4)	2 (0,5)	2 (0,5)	2 (0,5)	2 (0,4)
Duration (Receivers), median (IQR)								3 (2,7)	3 (2,7)	3 (2,8)	3 (2,7)	3 (2,8)
Basic cardiovascular support												
Number, n (%)								751 (81.6)	781 (83.5)	1,006 (83.6)	1,192 (85.1)	1,333 (86.1)
Duration (All), median (IQR)								2 (1,5)	3 (1,6)	3 (1,6)	3 (1,6)	3 (2,6)
Duration (Receivers), median (IQR)								3 (2,6)	4 (2,7)	4 (2,7)	3 (2,6)	3 (2,7)
Advanced cardiovascular support												
Number, n (%)								385 (41.8)	354 (37.9)	440 (36.5)	538 (38.4)	473 (30.6)
Duration (All), median (IQR)								0 (0,1)	0 (0,1)	0 (0,2)	0 (0,2)	0 (0,1)

Duration (Receivers), median (IQR)								2 (1,3)	2 (1,3)	2 (1,4)	2 (1,4)	2 (1,4)
Renal support												
Number, n (%)								219 (23.8)	217 (23.2)	249 (20.7)	302 (21.6)	303 (19.6)
Duration (All), median (IQR)								0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)								3 (2,6)	4 (2,7)	4 (2,8)	3 (2,6)	4 (2,7)
Critical care unit length of stay												
All, mean (sd)	4.7 (5.8)	6.2 (13.1)	5.1 (6.8)	4.9 (6.1)	5.5 (7.5)	5.7 (8.7)	5.5 (8.0)	5.5 (7.4)	5.5 (7.2)	6.5 (9.5)	5.6 (7.5)	5.6 (7.3)
Unit non-survivors, median (IQR)	2.2 (0.7,5.4)	2.1 (0.9,6.9)	2.0 (0.8,6.2)	2.4 (0.8,5.9)	2.2 (0.8,6.9)	2.9 (1.0,6.8)	2.0 (0.9,7.0)	2.1 (0.7,7.1)	2.1 (0.9,6.1)	2.8 (1.0,7.5)	3.1 (0.9,7.1)	2.7 (1.0,7.3)
Unit survivors, median (IQR)	2.7 (1.0,6.2)	2.9 (1.3,6.3)	2.5 (1.1,7.3)	2.8 (1.1,6.5)	2.8 (1.5,6.7)	2.6 (1.2,6.2)	3.0 (1.5,6.9)	3.0 (1.4,6.5)	3.0 (1.6,6.8)	3.6 (1.7,8.1)	3.1 (1.6,6.8)	3.1 (1.5,7.1)
Acute hospital length of stay*												
All, mean (sd)	24.2 (33.1)	24.9 (29.5)	22.3 (26.2)	21.8 (24.0)	23.9 (27.1)	24.4 (30.3)	22.4 (29.3)	22.5 (26.6)	23.2 (33.6)	24.5 (31.3)	23.4 (29.4)	23.1 (26.9)
Unit non-survivors, median (IQR)	8.0 (4.0,19.0)	10.0 (3.0,23.0)	10.0 (4.0,21.0)	9.5 (3.0,21.0)	10.0 (3.0,21.5)	10.0 (4.0,20.0)	10.0 (3.0,20.0)	9.0 (3.0,21.0)	9.0 (3.0,20.0)	10.0 (4.0,20.0)	10.0 (4.0,21.0)	11.0 (3.0,22.0)
Unit survivors, median (IQR)	26.0 (13.0,45.0)	24.0 (13.0,45.0)	23.5 (12.0,44.0)	23.5 (11.0,37.5)	27.0 (13.0,48.0)	22.0 (12.0,44.0)	19.0 (10.0,37.0)	20.0 (9.0,35.0)	22.0 (12.0,36.0)	20.0 (11.0,43.0)	19.0 (10.0,34.0)	19.0 (9.0,39.0)

*Excluding readmissions

Table S4a: Geographical area (Midlands) – Demographics and case mix

	1998	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**
Number of admissions, n (%) {CI} [N]	167 (1.4) {1.2,1.7} [11,738]	161 (1.3) {1.1,1.5} [12,728]	164 (1.3) {1.1,1.5} [12,525]	286 (1.9) {1.7,2.2} [14,813]	356 (2.1) {1.9,2.4} [16,727]	531 (2.4) {2.2,2.6} [22,080]	546 (2.4) {2.2,2.6} [22,779]	430 (1.9) {1.7,2.1} [22,654]	558 (2.5) {2.3,2.8} [21,921]	640 (2.8) {2.6,3.0} [23,227]	702 (2.9) {2.7,3.1} [24,597]	769 (2.9) {2.7,3.2} [26,084]	777 (2.8) {2.7,3.1} [27,290]	875 (2.8) {2.6,3.0} [30,937]	900 (2.7) {2.5,2.9} [33,356]
Extrapolated number of admissions, n (%) [N]	250 (1.4) [17,950]	250 (1.3) [19,000]	250 (1.3) [18,050]	400 (1.9) [20,400]	450 (2.1) [20,850]	550 (2.4) [23,300]	600 (2.4) [24,400]	500 (1.9) [25,650]	650 (2.5) [26,050]	750 (2.8) [26,600]	800 (2.9) [27,250]	850 (2.9) [28,350]	850 (2.8) [30,200]	950 (2.8) [33,050]	950 (2.7) [36,150]
Age, mean (SD)	51.9 (13.9)	50.2 (13.3)	53.0 (13.7)	51.9 (12.5)	53.0 (13.2)	53.3 (13.4)	53.1 (13.0)	53.4 (12.3)	51.8 (12.4)	52.9 (13.1)	52.8 (12.7)	52.6 (12.2)	53.0 (12.7)	53.0 (12.1)	53.6 (12.9)
Number of males, n (%)	88 (52.7)	102 (63.4)	106 (64.6)	172 (60.1)	211 (59.3)	322 (60.6)	328 (60.1)	265 (61.6)	347 (62.2)	383 (59.8)	444 (63.2)	494 (64.2)	481 (61.9)	528 (60.3)	566 (62.9)

Ethnicity , n (%)															
White											587 (86.6)	681 (88.6)	707 (91.0)	785 (89.7)	814 (90.4)
Asian											43 (6.3)	47 (6.1)	32 (4.1)	54 (6.2)	51 (5.7)
Black											4 (0.6)	7 (0.9)	9 (1.2)	4 (0.5)	7 (0.8)
Other											6 (0.9)	11 (1.4)	6 (0.8)	7 (0.8)	14 (1.6)
Not stated											38 (5.6)	23 (3.0)	23 (3.0)	25 (2.9)	14 (1.6)
Deprivation IMD quintile , n (%)															
1 (least deprived)	19 (11.7)	14 (9.3)	25 (15.9)	46 (16.4)	45 (13.0)	81 (15.6)	81 (15.1)	65 (15.3)	80 (14.4)	89 (14.1)	113 (16.2)	119 (15.5)	112 (14.5)	121 (14.0)	137 (15.4)
2	28 (17.2)	22 (14.6)	25 (15.9)	31 (11.1)	63 (18.3)	92 (17.8)	100 (18.6)	67 (15.7)	102 (18.4)	120 (19.0)	140 (20.1)	153 (20.0)	136 (17.6)	125 (14.5)	153 (17.2)
3	35 (21.5)	27 (17.9)	27 (17.2)	59 (21.1)	77 (22.3)	94 (18.1)	103 (19.1)	81 (19.0)	83 (15.0)	120 (19.0)	148 (21.3)	154 (20.1)	148 (19.1)	202 (23.4)	190 (21.4)
4	36 (22.1)	34 (22.5)	38 (24.2)	64 (22.9)	72 (20.9)	95 (18.3)	109 (20.3)	94 (22.1)	119 (21.5)	132 (20.9)	140 (20.1)	158 (20.6)	163 (21.1)	198 (22.9)	160 (18.0)
5 (most deprived)	45 (27.6)	54 (35.8)	42 (26.8)	80 (28.6)	88 (25.5)	156 (30.1)	145 (27.0)	119 (27.9)	170 (30.7)	171 (27.1)	155 (22.3)	182 (23.8)	214 (27.7)	218 (25.2)	247 (27.8)
APACHE II Acute Physiology Score, mean (SD)	15.7 (7.8)	15.0 (8.4)	16.6 (7.5)	16.0 (8.1)	15.2 (8.1)	15.4 (7.3)	15.5 (7.6)	15.5 (7.2)	14.9 (7.6)	15.2 (7.1)	14.4 (6.8)	14.6 (7.0)	14.7 (5.9)	14.0 (6.6)	14.3 (6.5)
APACHE II score, mean (SD)	19.7 (8.2)	18.5 (8.7)	20.6 (8.2)	20.2 (8.8)	19.2 (8.5)	19.3 (7.7)	19.4 (8.1)	19.4 (7.8)	18.8 (8.0)	19.2 (7.4)	18.6 (7.4)	18.8 (7.5)	19.2 (6.8)	18.3 (7.4)	18.8 (7.2)
ICNARC physiology score, mean (SD)	23.0 (11.3)	25.0 (13.5)	24.9 (11.9)	24.7 (12.1)	22.9 (11.7)	23.2 (10.9)	22.8 (10.9)	22.5 (10.7)	22.2 (11.2)	22.3 (10.4)	21.5 (10.7)	21.6 (10.3)	21.9 (9.6)	21.2 (10.1)	20.8 (9.7)
Highest serum creatinine*, mean (SD)	175.3 (148.1)	166.5 (143.9)	178.4 (139.8)	177.5 (137.6)	166.8 (126.1)	180.7 (162.5)	168.0 (137.8)	163.7 (139.4)	158.1 (119.9)	162.2 (130.1)	165.5 (150.8)	172.5 (178.2)	155.2 (138.1)	148.3 (127.9)	155.1 (147.9)
Highest blood lactate, mean (SD)**											4.5 (4.3)	4.5 (4.3)	4.5 (4.1)	4.4 (4.2)	4.3 (4.2)

*Missing data for 37% of admissions

**Missing data for 11% of admissions

Table S4b: Geographical area (Midlands) – Outcomes

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012

Critical care unit mortality, deaths (%) {CI} [N]	77 (46.1) {38.7,53.7} [167]	72 (44.7) {37.3,52.4} [161]	91 (55.5) {47.8,62.9} [164]	125 (43.7) {38.1,49.5} [286]	145 (40.7) {35.8,45.9} [356]	205 (38.6) {34.6,42.8} [531]	202 (37.0) {33.1,41.1} [546]	154 (35.8) {31.4,40.5} [430]	200 (35.8) {32.0,39.9} [558]	204 (31.9) {28.4,35.6} [640]	217 (30.9) {27.6,34.4} [702]	248 (32.2) {29.0,35.6} [769]	246 (31.7) {28.5,35.0} [777]	249 (28.5) {25.6,31.5} [875]	248 (27.6) {24.7,30.6} [900]
Acute hospital mortality*, deaths (%) {CI} [N]	101 (63.9) {56.2,71.0} [158]	90 (58.8) {50.9,66.3} [153]	102 (65.8) {58.0,72.8} [155]	151 (59.0) {52.9,64.8} [256]	191 (57.0) {51.7,62.2} [335]	264 (54.3) {49.9,58.7} [486]	269 (53.7) {49.3,58.0} [501]	223 (54.9) {50.1,59.7} [406]	257 (49.2) {45.0,53.5} [522]	257 (44.5) {40.5,48.5} [578]	297 (45.3) {41.5,49.1} [656]	328 (46.4) {42.7,50.1} [707]	334 (46.5) {42.8,50.1} [719]	340 (41.5) {38.2,44.9} [819]	359 (42.1) {38.8,45.4} [853]
Extrapolated acute hospital mortality, deaths (%)	150 (63.9) [250]	150 (58.8) [250]	150 (65.8) [200]	200 (59.0) [350]	250 (57.0) [400]	300 (54.3) [500]	300 (53.7) [550]	250 (54.9) [450]	300 (49.2) [600]	300 (44.5) [650]	350 (45.3) [750]	350 (46.4) [750]	350 (46.5) [800]	350 (41.5) [900]	400 (42.1) [900]
Number of patients readmitted, n (%) [N]**	5 (6.8) [74]	5 (7.4) [68]	4 (7.5) [53]	17 (12.9) [132]	14 (7.8) [180]	32 (11.9) [270]	35 (11.8) [296]	21 (9.0) [233]	23 (7.5) [308]	39 (10.4) [374]	33 (7.8) [423]	42 (9.4) [447]	42 (9.4) [448]	51 (9.6) [532]	42 (7.5) [558]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S4c: Geographical area (Midlands) – Resource use

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support															
Number, n (%)											505 (71.9)	549 (71.4)	559 (71.9)	591 (67.5)	608 (67.6)
Duration (All), median (IQR)											2 (0,4)	2 (0,4)	2 (0,4)	2 (0,4)	2 (0,4)
Duration (Receivers), median (IQR)											2 (2,6)	3 (2,7)	3 (2,6)	3 (2,7)	3 (2,6)
Basic cardiovascular support															
Number, n (%)											595 (84.8)	669 (87.0)	665 (85.6)	784 (89.6)	798 (88.7)
Duration (All), median (IQR)											3 (1,5)	3 (2,6)	3 (2,6)	3 (2,6)	3 (2,6)
Duration (Receivers), median (IQR)											3 (2,6)	3 (2,6)	4 (2,6)	3 (2,6)	3 (2,6)

Advanced cardiovascular support Number, n (%)											278 (39.6)	272 (35.4)	257 (33.1)	261 (29.8)	295 (32.8)
Duration (All), median (IQR)											0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)
Duration (Receivers), median (IQR)											2 (1,3)	2 (1,3)	2 (1,3)	2 (1,3)	2 (1,4)
Renal support Number, n (%)											145 (20.7)	151 (19.6)	130 (16.7)	150 (17.1)	157 (17.4)
Duration (All), median (IQR)											0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)											3 (2,6)	3 (2,7)	4 (2,8)	3 (2,5)	3 (2,6)
Critical care unit length of stay															
All, mean (sd)	3.4 (4.6)	4.8 (6.8)	5.3 (7.6)	5.7 (8.2)	4.9 (7.5)	5.1 (6.8)	5.5 (7.5)	6.0 (11.2)	5.0 (7.2)	5.1 (6.9)	5.0 (7.3)	5.6 (7.8)	5.1 (6.6)	5.2 (6.7)	5.5 (8.1)
Unit non-survivors, median (IQR)	1.5 (0.7,4.2)	1.1 (0.4,3.3)	2.2 (0.8,6.1)	2.6 (0.8,7.6)	1.7 (0.9,6.1)	2.2 (0.7,6.0)	2.2 (0.8,7.5)	1.8 (0.7,7.3)	2.0 (0.7,5.9)	1.8 (0.6,5.7)	2.1 (0.7,5.3)	2.7 (0.8,7.1)	2.2 (0.7,4.8)	1.9 (0.6,7.1)	2.4 (0.8,6.9)
Unit survivors, median (IQR)	1.8 (0.8,3.9)	3.0 (1.1,6.9)	2.1 (0.9,6.1)	2.6 (1.1,6.1)	2.1 (1.0,4.8)	2.9 (1.1,6.4)	2.5 (1.1,6.2)	2.7 (1.2,6.6)	2.6 (1.3,6.1)	2.7 (1.3,6.2)	2.5 (1.4,5.7)	2.9 (1.3,6.1)	3.2 (1.5,6.3)	2.9 (1.5,6.1)	3.0 (1.5,6.3)
Acute hospital length of stay*															
All, mean (sd)	20.2 (35.8)	19.5 (38.9)	20.8 (29.2)	23.6 (28.4)	20.8 (25.7)	23.4 (31.7)	26.2 (32.2)	24.0 (31.4)	23.7 (35.1)	20.1 (22.3)	22.5 (25.9)	23.4 (28.3)	22.6 (27.2)	21.8 (25.2)	21.4 (23.2)
Unit non-survivors, median (IQR)	6.0 (2.0,16.0)	7.0 (2.0,16.0)	6.0 (2.5,16.0)	9.0 (3.0,19.0)	7.0 (3.0,17.0)	8.0 (3.0,15.0)	10.0 (3.0,22.0)	10.0 (4.0,22.0)	8.0 (3.0,18.5)	8.0 (3.0,17.0)	8.0 (3.0,22.0)	9.0 (4.0,20.0)	9.0 (3.0,17.0)	10.0 (3.0,21.0)	9.0 (3.0,19.0)

Unit survivors, median (IQR)	16.0 (10.0,41.0)	17.0 (11.0,33.0)	26.0 (14.0,40.0)	23.5 (13.0,49.0)	19.5 (14.0,35.0)	23.0 (13.0,43.0)	24.5 (15.0,42.0)	21.0 (11.0,38.0)	19.0 (10.0,38.0)	18.0 (10.0,31.0)	19.0 (10.0,34.0)	19.0 (11.0,37.0)	18.0 (11.0,37.0)	17.0 (9.0,33.0)	16.0 (9.0,32.0)

*Excluding readmissions

Table S5a: Geographical area (North) – Demographics and case mix

	1998	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**
Number of admissions, n (%) {CI} [N]	248 (2.5) {2.2,2.8} [10,118]	352 (3.2) {2.9,3.5} [11,128]	367 (3.1) {2.8,3.4} [11,839]	447 (3.0) {2.7,3.3} [15,065]	567 (2.9) {2.7,3.2} [19,421]	606 (3.1) {2.8,3.3} [19,802]	628 (2.9) {2.7,3.1} [21,816]	643 (2.9) {2.7,3.1} [22,197]	617 (2.8) {2.6,3.0} [22,165]	705 (3.1) {2.9,3.3} [22,638]	708 (3.0) {2.8,3.2} [23,936]	893 (3.3) {3.0,3.5} [27,475]	1,132 (3.4) {3.2,3.6} [33,431]	1,320 (3.6) {3.4,3.8} [36,603]	1,417 (3.6) {3.5,3.8} [38,913]
Extrapolated number of admissions, n (%) [N]	550 (2.5) [21,450]	650 (3.2) [20,900]	700 (3.1) [22,000]	700 (3.0) [23,800]	750 (2.9) [25,150]	800 (3.1) [26,200]	800 (2.9) [28,000]	800 (2.9) [28,050]	800 (2.8) [29,100]	950 (3.1) [30,400]	950 (3.0) [32,850]	1,150 (3.3) [34,900]	1,250 (3.4) [36,200]	1,400 (3.6) [38,900]	1,500 (3.6) [41,550]
Age, mean (SD)	47.7 (13.6)	49.8 (13.6)	50.3 (12.7)	50.6 (11.6)	51.2 (12.9)	51.8 (12.6)	51.8 (13.1)	51.7 (13.5)	51.3 (13.1)	52.2 (13.2)	53.6 (13.5)	52.4 (13.4)	52.7 (12.0)	52.2 (12.8)	52.5 (13.0)
Number of males, n (%)	145 (58.5)	219 (62.2)	227 (61.9)	286 (64.0)	333 (58.7)	351 (57.9)	362 (57.6)	393 (61.1)	348 (56.4)	403 (57.2)	417 (58.9)	525 (58.8)	679 (60.0)	812 (61.5)	879 (62.0)
Ethnicity , n (%)															
White											498 (95.6)	846 (94.9)	1,081 (95.5)	1,261 (95.5)	1,352 (95.4)
Asian											12 (2.3)	21 (2.4)	27 (2.4)	34 (2.6)	33 (2.3)
Black											2 (0.4)	6 (0.7)	4 (0.4)	6 (0.5)	3 (0.2)
Other											3 (0.6)	10 (1.1)	13 (1.1)	12 (0.9)	16 (1.1)
Not stated											6 (1.2)	8 (0.9)	7 (0.6)	7 (0.5)	13 (0.9)
Deprivation IMD quintile , n (%)															
1 (least deprived)	20 (8.8)	38 (11.5)	42 (11.8)	41 (9.5)	71 (12.9)	68 (11.5)	51 (8.2)	65 (10.2)	60 (9.9)	54 (7.7)	47 (6.7)	62 (7.0)	96 (8.5)	131 (9.9)	116 (8.3)
2	42 (18.6)	45 (13.6)	40 (11.2)	45 (10.5)	54 (9.8)	76 (12.8)	95 (15.3)	78 (12.3)	71 (11.7)	106 (15.1)	73 (10.4)	103 (11.6)	140 (12.5)	152 (11.5)	189 (13.5)

3	19 (8.4)	50 (15.1)	59 (16.6)	71 (16.5)	75 (13.6)	91 (15.4)	77 (12.4)	96 (15.1)	81 (13.3)	84 (11.9)	106 (15.1)	115 (13.0)	169 (15.0)	173 (13.1)	201 (14.3)
4	49 (21.7)	61 (18.4)	56 (15.7)	84 (19.5)	109 (19.8)	106 (17.9)	101 (16.3)	111 (17.5)	106 (17.4)	137 (19.5)	154 (22.0)	160 (18.1)	206 (18.3)	256 (19.4)	305 (21.7)
5 (most deprived)	96 (42.5)	137 (41.4)	159 (44.7)	189 (44.0)	242 (43.9)	251 (42.4)	296 (47.7)	286 (45.0)	291 (47.8)	323 (45.9)	321 (45.8)	445 (50.3)	512 (45.6)	606 (46.0)	592 (42.2)
APACHE II Acute Physiology Score, mean (SD)	16.1 (7.5)	15.5 (7.8)	16.2 (7.4)	15.9 (7.8)	16.5 (7.4)	16.8 (7.9)	16.9 (8.0)	16.4 (8.0)	16.2 (7.3)	16.5 (7.2)	15.0 (6.9)	15.4 (6.9)	15.3 (7.0)	15.3 (6.9)	14.9 (6.7)
APACHE II score, mean (SD)	20.6 (8.2)	20.4 (8.3)	21.2 (7.8)	20.9 (8.4)	21.3 (8.0)	21.6 (8.8)	21.5 (8.9)	20.8 (8.7)	20.4 (8.1)	21.1 (7.9)	19.6 (7.4)	20.0 (7.5)	19.9 (7.7)	20.1 (7.6)	19.8 (7.4)
ICNARC physiology score, mean (SD)	22.0 (10.6)	22.1 (11.6)	23.2 (11.4)	22.7 (12.0)	23.5 (11.5)	23.9 (10.6)	23.9 (11.5)	23.6 (11.3)	22.9 (10.7)	23.1 (10.3)	22.2 (10.0)	22.8 (10.0)	22.3 (9.9)	22.2 (9.9)	21.4 (9.7)
Highest serum creatinine*, mean (SD)	176.6 (137.9)	168.3 (132.8)	159.4 (120.7)	163.1 (134.2)	166.0 (141.5)	167.4 (138.2)	161.5 (138.3)	165.8 (133.8)	148.9 (116.4)	161.8 (135.4)	160.4 (143.5)	163.6 (133.0)	158.3 (132.1)	158.1 (154.3)	147.2 (134.9)
Highest blood lactate, mean (SD)**											4.7 (4.7)	4.6 (4.5)	4.9 (4.5)	4.6 (4.4)	4.4 (4.2)

*Missing data for 21% of admissions

**Missing data for 15% of admissions

Table S5b: Geographical area (North) – Outcomes

	1998	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**
Critical care unit mortality, deaths (%) {CI} [N]	84 (33.9) {28.3,40.0} [248]	131 (37.2) {32.3,42.4} [352]	138 (37.6) {32.8,42.7} [367]	160 (35.8) {31.5,40.3} [447]	212 (37.4) {33.5,41.4} [567]	233 (38.4) {34.7,42.4} [606]	239 (38.1) {34.3,41.9} [628]	250 (38.9) {35.2,42.7} [643]	228 (37.0) {33.2,40.8} [617]	265 (37.6) {34.1,41.2} [705]	254 (35.9) {32.4,39.5} [708]	345 (38.6) {35.5,41.9} [893]	358 (31.6) {29.0,34.4} [1,132]	415 (31.4) {29.0,34.0} [1,320]	454 (32.0) {29.7,34.5} [1,417]
Acute hospital mortality*, deaths (%) {CI} [N]	110 (50.2) {43.7,56.8} [219]	166 (51.4) {46.0,56.8} [323]	163 (50.6) {45.2,56.0} [322]	198 (51.7) {46.7,56.7} [383]	275 (54.0) {49.7,58.3} [509]	298 (54.3) {50.1,58.4} [549]	307 (52.5) {48.4,56.5} [585]	316 (52.4) {48.4,56.4} [603]	306 (52.7) {48.6,56.7} [581]	353 (53.9) {50.1,57.7} [655]	336 (50.8) {47.0,54.5} [662]	429 (51.1) {47.7,54.4} [840]	497 (47.2) {44.2,50.2} [1,054]	571 (46.2) {43.4,48.9} [1,237]	600 (46.0) {43.4,48.8} [1,303]
Extrapolated acute hospital mortality, deaths (%) [N]	250 (50.2) [450]	300 (51.4) [600]	300 (50.6) [600]	300 (51.7) [600]	350 (54.0) [650]	400 (54.3) [750]	400 (52.5) [750]	400 (52.4) [750]	400 (52.7) [750]	450 (53.9) [900]	450 (50.8) [900]	550 (51.1) [1,050]	550 (47.2) [1,150]	600 (46.2) [1,300]	650 (46.0) [1,400]

Number of patients readmitted, n (%) [N]**	19 (15.6) [122]	23 (12.0) [192]	28 (15.2) [184]	39 (17.5) [223]	43 (14.5) [297]	40 (13.0) [307]	33 (9.9) [332]	28 (8.3) [337]	35 (10.6) [329]	40 (11.0) [364]	41 (11.1) [371]	42 (9.3) [450]	67 (10.4) [643]	73 (9.6) [758]	82 (10.2) [804]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S5c: Geographical area (North) – Resource use

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support															
Number, n (%)											538 (76.0)	608 (68.1)	766 (67.7)	845 (64.0)	911 (64.3)
Duration (All), median (IQR)											2 (0,5)	2 (0,6)	2 (0,5)	2 (0,5)	2 (0,5)
Duration (Receivers), median (IQR)											3 (2,7)	4 (2,9)	3 (2,7)	3 (2,7)	3 (2,8)
Basic cardiovascular support															
Number, n (%)											634 (89.5)	776 (86.9)	987 (87.2)	1,159 (87.8)	1,249 (88.1)
Duration (All), median (IQR)											3 (1,6)	3 (2,7)	3 (2,6)	3 (2,6)	3 (2,6)
Duration (Receivers), median (IQR)											3 (2,7)	4 (2,8)	3 (2,7)	3 (2,7)	3 (2,7)
Advanced cardiovascular support															
Number, n (%)											358 (50.6)	261 (29.2)	305 (26.9)	343 (26.0)	332 (23.4)
Duration (All), median (IQR)											0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,0)
Duration (Receivers), median (IQR)											2 (1,3)	2 (1,3)	2 (1,3)	2 (1,3)	2 (1,3)
Renal support															
Number, n (%)											280 (39.5)	146 (16.3)	176 (15.5)	220 (16.7)	227 (16.0)

Duration (All), median (IQR)											0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)											3 (2,5)	3 (2,6)	4 (2,6)	3 (2,7)	3 (2,6)
Critical care unit length of stay															
All, mean (sd)	4.0 (6.2)	4.3 (11.9)	4.0 (6.1)	4.4 (6.4)	5.1 (7.5)	5.1 (7.2)	4.5 (5.4)	4.6 (6.1)	5.1 (7.9)	4.7 (6.9)	5.5 (7.2)	5.6 (7.6)	5.1 (6.9)	5.4 (7.8)	5.7 (7.4)
Unit non-survivors, median (IQR)	2.2 (0.7,7.2)	1.8 (0.8,5.6)	2.4 (1.0,5.7)	2.3 (0.8,5.5)	2.5 (0.9,6.5)	2.2 (1.0,5.4)	2.0 (0.6,6.8)	2.1 (0.8,5.6)	2.3 (0.8,6.0)	1.8 (0.7,4.8)	2.4 (0.8,6.3)	2.8 (1.0,6.9)	2.0 (0.7,6.1)	1.9 (0.7,5.9)	2.5 (0.9,7.1)
Unit survivors, median (IQR)	1.6 (0.8,3.9)	1.2 (0.8,3.8)	1.6 (1.0,3.9)	1.8 (0.9,5.0)	2.1 (1.0,5.7)	2.7 (1.0,6.6)	2.4 (1.0,5.6)	2.5 (1.0,6.0)	2.5 (1.1,6.2)	2.4 (1.1,5.4)	2.8 (1.3,7.5)	2.7 (1.2,7.0)	2.7 (1.3,6.2)	3.0 (1.3,6.9)	3.0 (1.5,7.0)
Acute hospital length of stay*															
All, mean (sd)	23.8 (26.7)	26.3 (34.4)	27.8 (35.2)	23.5 (25.5)	23.0 (28.2)	22.9 (27.1)	23.1 (27.2)	22.6 (25.7)	22.2 (28.2)	21.3 (24.9)	24.0 (29.8)	21.3 (26.8)	23.0 (28.1)	22.8 (28.0)	22.1 (25.7)
Unit non-survivors, median (IQR)	9.0 (3.0,16.0)	10.0 (3.0,21.0)	8.5 (3.0,17.0)	9.0 (3.0,20.0)	8.0 (3.0,20.0)	7.0 (3.0,17.0)	9.0 (3.0,19.0)	8.0 (3.0,16.0)	8.0 (3.0,18.0)	8.0 (3.0,16.0)	9.0 (3.0,20.0)	8.0 (3.0,18.0)	8.0 (3.0,19.0)	9.0 (3.0,20.0)	8.0 (3.0,18.0)
Unit survivors, median (IQR)	22.0 (13.0,47.0)	21.0 (13.0,39.0)	28.5 (15.0,47.0)	23.0 (14.0,39.0)	23.0 (14.0,38.0)	24.0 (14.0,41.0)	24.0 (14.0,41.0)	22.0 (14.0,43.0)	20.0 (12.0,35.0)	22.0 (13.0,37.0)	23.0 (12.0,39.5)	19.0 (10.0,37.0)	20.0 (11.0,38.0)	20.0 (11.0,36.0)	19.0 (10.0,36.0)

*Excluding readmissions

Table S6a: Geographical area (Wales) – Demographics and case mix

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Number of admissions, n (%) {CI} [N]	50 (1.3) {1.0,1.7} [3,939]	39 (0.9) {0.7,1.3} [4,143]	62 (1.6) {1.3,2.1} [3,826]	104 (2.0) {1.7,2.5} [5,116]	112 (1.8) {1.5,2.2} [6,089]	137 (2.0) {1.7,2.3} [6,964]	191 (2.7) {2.3,3.1} [7,096]	195 (2.3) {2.0,2.6} [8,561]	213 (2.5) {2.2,2.8} [8,547]	213 (2.4) {2.1,2.7} [9,003]

Extrapolated number of admissions, n (%) [N]	100 (1.3) [7,450]	50 (0.9) [7,250]	150 (1.6) [7,850]	150 (2.0) [7,850]	150 (1.8) [8,650]	200 (2.0) [9,500]	250 (2.7) [8,750]	200 (2.3) [8,650]	200 (2.5) [8,700]	250 (2.4) [9,650]
Age, mean (SD)	55.4 (14.5)	56.9 (11.1)	53.3 (12.3)	53.3 (12.7)	54.6 (13.1)	53.4 (13.1)	51.0 (11.6)	52.6 (13.5)	53.2 (11.9)	53.3 (11.9)
Number of males, n (%)	30 (60.0)	26 (66.7)	38 (61.3)	56 (53.8)	63 (56.3)	87 (63.5)	118 (61.8)	112 (57.4)	125 (58.7)	133 (62.4)
Ethnicity , n (%)										
White						114 (100.0)	185 (96.9)	195 (100.0)	202 (94.8)	207 (97.2)
Asian						0 (0.0)	3 (1.6)	0 (0.0)	5 (2.3)	3 (1.4)
Black						0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	3 (1.4)
Other						0 (0.0)	1 (0.5)	0 (0.0)	3 (1.4)	0 (0.0)
Not stated						0 (0.0)	2 (1.0)	0 (0.0)	2 (0.9)	0 (0.0)
Deprivation IMD quintile , n (%)										
1 (least deprived)	4 (8.0)	3 (7.7)	4 (6.5)	5 (4.9)	19 (17.0)	17 (12.4)	21 (11.2)	24 (12.4)	29 (13.7)	28 (13.1)
2	8 (16.0)	9 (23.1)	9 (14.5)	13 (12.7)	9 (8.0)	17 (12.4)	22 (11.7)	27 (13.9)	29 (13.7)	35 (16.4)
3	9 (18.0)	4 (10.3)	15 (24.2)	21 (20.6)	30 (26.8)	20 (14.6)	23 (12.2)	46 (23.7)	37 (17.5)	30 (14.1)
4	13 (26.0)	5 (12.8)	18 (29.0)	31 (30.4)	18 (16.1)	35 (25.5)	34 (18.1)	31 (16.0)	47 (22.3)	51 (23.9)
5 (most deprived)	16 (32.0)	18 (46.2)	16 (25.8)	32 (31.4)	36 (32.1)	48 (35.0)	88 (46.8)	66 (34.0)	69 (32.7)	69 (32.4)
APACHE II Acute Physiology Score, mean (SD)	17.0 (8.2)	14.6 (6.4)	16.1 (7.8)	16.3 (8.2)	14.7 (6.8)	15.7 (7.8)	15.5 (7.2)	14.3 (5.8)	15.3 (7.0)	13.5 (6.0)
APACHE II score, mean (SD)	20.8 (8.6)	19.4 (6.1)	19.9 (8.6)	19.7 (8.8)	18.6 (7.3)	19.8 (8.4)	19.5 (7.8)	18.7 (6.4)	19.8 (7.5)	18.2 (6.5)
ICNARC physiology score, mean (SD)	23.1 (9.6)	24.1 (10.4)	22.5 (8.5)	22.1 (11.1)	21.5 (10.4)	22.3 (10.5)	22.6 (10.5)	21.8 (10.2)	22.8 (9.7)	20.6 (9.0)
Highest serum creatinine*, mean (SD)	240.0 (284.2)	200.1 (193.5)	171.7 (183.7)	225.3 (198.9)	140.9 (124.2)	143.1 (112.1)	164.1 (183.7)	170.1 (153.5)	152.3 (133.8)	139.7 (131.7)
Highest blood lactate, mean (SD)**						3.4 (3.5)	4.4 (4.9)	4.2 (4.0)	4.6 (4.6)	4.0 (4.0)

*Missing data for 23% of admissions
**Missing data for 18% of admissions

Table S6b: Geographical area (Wales) – Outcomes

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Critical care unit mortality, deaths (%) {CI} [N]	24 (48.0) {34.8,61.5} [50]	16 (41.0) {27.1,56.6} [39]	22 (35.5) {24.7,47.9} [62]	39 (37.5) {28.8,47.1} [104]	41 (36.6) {28.3,45.8} [112]	50 (36.5) {28.9,44.8} [137]	63 (33.0) {26.7,39.9} [191]	67 (34.4) {28.1,41.3} [195]	75 (35.2) {29.1,41.8} [213]	75 (35.2) {29.1,41.8} [213]

Acute hospital mortality*, deaths (%) {CI}	32 (71.1) {56.6,82.3} [45]	25 (69.4) {53.1,82.0} [36]	34 (59.6) {46.7,71.4} [57]	61 (61.6) {51.8,70.6} [99]	58 (54.7) {45.2,63.9} [106]	70 (56.5) {47.7,64.9} [124]	96 (51.6) {44.5,58.7} [186]	94 (50.0) {42.9,57.1} [188]	96 (48.7) {41.8,55.7} [197]	105 (50.5) {43.7,57.2} [208]
Extrapolated acute hospital mortality, deaths (%) [N]	50 (71.1) [100]	50 (69.4) [50]	50 (59.6) [100]	100 (61.6) [150]	100 (54.7) [150]	100 (56.5) [150]	100 (51.6) [250]	100 (50.0) [200]	100 (48.7) [200]	100 (50.5) [200]
Number of patients readmitted, n (%) [N]**	3 (12.5) [24]	3 (15.8) [19]	4 (12.5) [32]	6 (12.0) [50]	5 (8.5) [59]	11 (17.7) [62]	5 (4.8) [105]	8 (7.2) [111]	15 (13.2) [114]	6 (5.1) [117]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S6c: Geographical area (Wales) – Resource use

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support										
Number, n (%)						86 (62.8)	117 (61.3)	118 (60.5)	135 (63.4)	123 (57.7)
Duration (All), median (IQR)						1 (0,3)	2 (0,4)	1 (0,4)	2 (0,4)	1 (0,4)
Duration (Receivers), median (IQR)						3 (2,8)	3 (2,9)	3 (2,7)	3 (2,7)	3 (2,8)
Basic cardiovascular support										
Number, n (%)						127 (92.7)	168 (88.0)	174 (89.2)	185 (86.9)	198 (93.0)
Duration (All), median (IQR)						3 (2,6)	3 (2,7)	3 (2,7)	3 (1,6)	3 (2,6)
Duration (Receivers), median (IQR)						3 (2,6)	3 (2,7)	4 (2,8)	3 (2,7)	3 (2,6)
Advanced cardiovascular support										
Number, n (%)						42 (30.7)	54 (28.3)	32 (16.4)	37 (17.4)	23 (10.8)
Duration (All), median (IQR)						0 (0,0)	0 (0,1)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)						2 (1,5)	2 (1,4)	2 (1,3)	2 (2,4)	3 (2,5)
Renal support										

Number, n (%)						35 (25.5)	29 (15.2)	31 (15.9)	39 (18.3)	30 (14.1)
Duration (All), median (IQR)						0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)						3 (2,6)	3 (2,5)	5 (2,10)	4 (2,6)	3 (2,5)
Critical care unit length of stay										
All, mean (sd)	5.3 (6.1)	3.0 (3.4)	5.4 (7.1)	4.1 (6.4)	3.3 (3.3)	4.7 (5.7)	5.8 (8.2)	6.6 (10.6)	5.8 (7.3)	5.4 (7.5)
Unit non-survivors, median (IQR)	3.7 (1.3,7.0)	1.2 (0.2,2.6)	2.7 (0.9,6.6)	2.2 (0.3,5.4)	2.4 (0.8,4.3)	1.8 (0.9,7.8)	2.1 (0.6,7.1)	2.1 (0.8,5.5)	3.0 (1.1,8.9)	2.9 (1.0,6.9)
Unit survivors, median (IQR)	2.8 (1.5,7.9)	2.4 (1.6,5.2)	3.1 (1.1,6.1)	1.8 (0.8,3.3)	2.4 (1.1,4.7)	2.8 (1.1,5.5)	2.8 (1.4,6.8)	3.1 (1.6,9.0)	3.2 (1.8,6.8)	3.2 (1.4,5.4)
Acute hospital length of stay*										
All, mean (sd)	22.6 (27.9)	20.0 (18.8)	31.1 (35.2)	25.6 (28.2)	28.6 (30.8)	25.2 (28.4)	25.0 (22.0)	27.8 (66.1)	20.3 (18.6)	24.9 (27.8)
Unit non-survivors, median (IQR)	8.5 (6.0,19.0)	11.0 (4.0,26.0)	15.0 (5.0,35.0)	13.0 (7.0,27.0)	9.0 (5.0,17.0)	9.5 (3.0,21.0)	10.0 (4.0,27.0)	13.0 (5.0,21.0)	13.0 (6.0,22.0)	13.0 (7.0,27.0)
Unit survivors, median (IQR)	17.0 (9.0,59.0)	18.0 (10.0,42.0)	25.0 (13.0,38.0)	25.5 (8.5,46.5)	31.5 (12.0,62.0)	30.0 (17.0,50.0)	25.0 (12.5,44.5)	15.0 (10.0,36.0)	17.5 (9.0,30.0)	20.0 (9.0,34.0)

*Excluding readmissions

Table S7a: Geographical area (Northern Ireland) – Demographics and case mix

	2001	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**
Number of admissions, n (%) {CI} [N]	46 (2.6) {2.0,3.5} [1,750]	44 (2.1) {1.5,2.7} [2,141]	56 (2.0) {1.5,2.5} [2,850]	70 (2.4) {1.9,3.0} [2,961]	71 (2.2) {1.8,2.8} [3,166]	94 (2.7) {2.2,3.2} [3,534]	87 (2.5) {2.1,3.1} [3,415]	102 (2.6) {2.1,3.1} [3,950]	139 (3.2) {2.7,3.8} [4,313]	124 (2.7) {2.3,3.2} [4,540]	145 (3.0) {2.5,3.5} [4,862]	129 (2.5) {2.1,3.0} [5,063]
Extrapolated number of admissions, n (%) [N]	100 (2.6) [3,350]	50 (2.1) [3,150]	50 (2.0) [3,500]	100 (2.4) [3,550]	100 (2.2) [3,800]	100 (2.7) [4,000]	100 (2.5) [3,950]	100 (2.6) [4,350]	150 (3.2) [4,300]	100 (2.7) [4,550]	150 (3.0) [4,850]	150 (2.5) [5,050]
Age, mean (SD)	49.0 (12.3)	53.4 (11.0)	51.2 (12.1)	52.3 (12.6)	52.7 (12.9)	53.1 (11.7)	50.0 (9.5)	52.0 (12.3)	52.8 (12.3)	53.2 (11.2)	52.5 (10.9)	53.8 (11.7)
Number of males, n (%)	36 (78.3)	19 (43.2)	41 (73.2)	46 (65.7)	45 (63.4)	58 (61.7)	51 (58.6)	62 (60.8)	86 (61.9)	71 (57.3)	92 (63.4)	84 (65.1)
Ethnicity , n (%)												
White								94 (92.2)	138 (99.3)	124 (100.0)	145 (100.0)	126 (97.7)
Asian								0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)

Black								0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other								0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.8)
Not stated								8 (7.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Deprivation IMD quintile , n (%)												
1 (least deprived)	4 (8.9)	4 (9.1)	5 (9.1)	8 (11.6)	9 (13.2)	10 (10.6)	10 (11.5)	14 (13.9)	14 (10.1)	13 (10.5)	14 (9.7)	11 (8.6)
2	6 (13.3)	11 (25.0)	8 (14.5)	8 (11.6)	6 (8.8)	13 (13.8)	13 (14.9)	10 (9.9)	26 (18.8)	23 (18.5)	20 (13.8)	22 (17.2)
3	6 (13.3)	3 (6.8)	5 (9.1)	12 (17.4)	11 (16.2)	14 (14.9)	12 (13.8)	11 (10.9)	23 (16.7)	20 (16.1)	23 (15.9)	21 (16.4)
4	8 (17.8)	12 (27.3)	12 (21.8)	13 (18.8)	18 (26.5)	17 (18.1)	20 (23.0)	24 (23.8)	27 (19.6)	18 (14.5)	30 (20.7)	27 (21.1)
5 (most deprived)	21 (46.7)	14 (31.8)	25 (45.5)	28 (40.6)	24 (35.3)	40 (42.6)	32 (36.8)	42 (41.6)	48 (34.8)	50 (40.3)	58 (40.0)	47 (36.7)
APACHE II Acute Physiology Score, mean (SD)	17.6 (8.6)	18.4 (6.7)	18.5 (7.4)	17.7 (7.5)	15.6 (7.8)	17.7 (7.1)	16.6 (7.8)	16.6 (7.8)	15.6 (6.9)	15.1 (6.8)	14.7 (7.2)	15.8 (6.8)
APACHE II score, mean (SD)	20.8 (8.8)	22.3 (8.0)	22.2 (8.0)	22.2 (8.5)	19.6 (8.6)	22.0 (7.8)	20.0 (8.3)	21.0 (8.8)	19.8 (7.4)	19.6 (7.4)	19.7 (7.8)	21.0 (7.5)
ICNARC physiology score, mean (SD)	25.7 (13.1)	27.1 (11.1)	27.8 (12.1)	25.5 (10.1)	23.2 (11.0)	25.0 (10.1)	24.4 (11.5)	23.5 (12.6)	23.6 (9.8)	24.5 (10.7)	22.1 (10.2)	23.1 (10.0)
Highest serum creatinine*, mean (SD)	170.4 (122.0)	187.4 (177.7)	156.2 (98.1)	189.9 (174.2)	133.6 (93.6)	170.4 (155.4)	134.8 (82.9)	119.3 (91.4)	145.1 (110.2)	147.1 (119.4)	134.4 (115.8)	153.3 (139.2)
Highest blood lactate, mean (SD)								4.3 (4.0)	5.6 (5.3)	5.1 (5.0)	4.7 (4.8)	4.6 (4.2)

*Missing data for 14% of admissions

Table S7b: Geographical area (Northern Ireland) – Outcomes

	2001	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**
Critical care unit mortality, deaths (%) {CI} [N]	23 (50.0) {36.1,63.9} [46]	25 (56.8) {42.2,70.3} [44]	23 (41.1) {29.2,54.1} [56]	31 (44.3) {33.2,55.9} [70]	20 (28.2) {19.0,39.5} [71]	35 (37.2) {28.1,47.3} [94]	29 (33.3) {24.3,43.8} [87]	46 (45.1) {35.8,54.8} [102]	47 (33.8) {26.5,42.0} [139]	44 (35.5) {27.6,44.2} [124]	40 (27.6) {21.0,35.4} [145]	48 (37.2) {29.4,45.8} [129]
Acute hospital mortality*, deaths (%) {CI} [N]	26 (57.8) {43.3,71.0} [45]	29 (69.0) {54.0,80.9} [42]	31 (57.4) {44.2,69.7} [54]	43 (68.3) {56.0,78.4} [63]	27 (44.3) {32.5,56.7} [61]	46 (55.4) {44.7,65.6} [83]	37 (45.7) {35.3,56.5} [81]	55 (56.7) {46.8,66.1} [97]	65 (50.4) {41.9,58.9} [129]	63 (53.4) {44.4,62.1} [118]	60 (44.8) {36.6,53.2} [134]	68 (58.1) {49.1,66.7} [117]

Extrapolated acute hospital mortality, deaths (%) [N]	50 (57.8) [100]	50 (69.0) [50]	50 (57.4) [50]	50 (68.3) [100]	50 (44.3) [50]	50 (55.4) [100]	50 (45.7) [100]	50 (56.7) [100]	50 (50.4) [150]	50 (53.4) [100]	50 (44.8) [150]	50 (58.1) [100]
Number of patients readmitted, n (%) [N]**	2 (10.5) [19]	1 (6.7) [15]	2 (6.7) [30]	6 (22.2) [27]	6 (15.4) [39]	9 (20.0) [45]	5 (10.0) [50]	5 (10.9) [46]	10 (11.8) [85]	8 (11.9) [67]	9 (10.8) [83]	9 (14.1) [64]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S7c: Geographical area (Northern Ireland) – Resource use

	2001	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**
Advanced respiratory support												
Number, n (%)								76 (74.5)	102 (73.4)	94 (75.8)	103 (71.0)	88 (68.2)
Duration (All), median (IQR)								2 (0,7)	3 (0,7)	3 (1,7)	2 (0,5)	2 (0,6)
Duration (Receivers), median (IQR)								4 (2,9)	5 (2,9)	5 (2,8)	4 (2,6)	4 (2,9)
Basic cardiovascular support												
Number, n (%)								92 (90.2)	128 (92.1)	115 (92.7)	120 (82.8)	116 (89.9)
Duration (All), median (IQR)								3 (2,6)	4 (2,9)	4 (2,7)	3 (1,6)	4 (2,9)
Duration (Receivers), median (IQR)								4 (2,7)	5 (2,9)	4 (3,8)	4 (2,7)	4 (2,10)
Advanced cardiovascular support												
Number, n (%)								35 (34.3)	45 (32.4)	30 (24.2)	37 (25.5)	38 (29.5)
Duration (All), median (IQR)								0 (0,2)	0 (0,1)	0 (0,0)	0 (0,1)	0 (0,1)

Duration (Receivers), median (IQR)								3 (2,5)	2 (1,3)	3 (2,4)	2 (2,3)	2 (1,4)
Renal support												
Number, n (%)								23 (22.5)	37 (26.6)	28 (22.6)	24 (16.6)	30 (23.3)
Duration (All), median (IQR)								0 (0,0)	0 (0,1)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)								3 (2,5)	4 (3,6)	5 (2,8)	4 (3,5)	5 (2,8)
Critical care unit length of stay												
All, mean (sd)	6.4 (7.7)	6.5 (6.8)	7.2 (12.8)	7.3 (10.3)	6.1 (10.4)	6.7 (7.3)	8.5 (9.9)	5.7 (7.4)	6.4 (6.4)	6.5 (9.7)	5.4 (5.8)	6.6 (9.7)
Unit non-survivors, median (IQR)	5.4 (1.6,13.3)	6.8 (1.2,9.9)	3.5 (0.6,6.0)	3.9 (1.2,9.4)	1.7 (0.8,5.9)	3.0 (1.3,10.4)	4.2 (1.6,13.6)	4.9 (1.5,8.8)	5.6 (1.5,9.5)	4.1 (1.6,7.8)	3.2 (1.4,6.4)	2.7 (0.9,7.5)
Unit survivors, median (IQR)	2.6 (0.8,4.8)	3.2 (1.3,9.2)	4.0 (1.7,6.4)	4.0 (1.8,8.4)	3.5 (1.1,6.1)	4.7 (1.7,10.7)	3.9 (2.1,12.1)	2.7 (1.2,5.2)	3.8 (2.2,8.5)	3.4 (1.9,8.7)	3.2 (1.8,7.0)	4.4 (1.6,9.4)
Acute hospital length of stay*												
All, mean (sd)	19.1 (22.2)	12.3 (9.6)	21.3 (26.1)	17.7 (22.2)	21.8 (30.2)	22.7 (33.2)	21.5 (25.0)	25.8 (31.8)	21.8 (23.8)	20.9 (24.6)	19.1 (22.2)	12.3 (9.6)
Unit non-survivors, median (IQR)	10.0 (4.5,20.5)	10.0 (3.0,15.0)	7.5 (4.0,14.0)	6.0 (2.0,18.0)	7.0 (1.0,17.0)	10.0 (2.0,16.0)	10.0 (2.5,24.0)	6.5 (3.0,17.0)	10.5 (3.0,20.5)	9.0 (3.0,21.0)	10.0 (4.5,20.5)	10.0 (3.0,15.0)
Unit survivors, median (IQR)	22.0 (9.0,38.0)	16.0 (9.0,25.0)	25.0 (15.0,46.0)	14.5 (6.0,29.0)	21.0 (11.0,41.5)	17.0 (10.0,43.0)	17.0 (8.0,32.0)	27.5 (12.0,45.0)	20.0 (11.0,37.0)	18.0 (9.0,36.0)	22.0 (9.0,38.0)	16.0 (9.0,25.0)

*Excluding readmissions

Table S8a: Alcohol related – Demographics and case mix

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Number of admissions, n (%) {CI} [N]	161 (28.9) {25.2,32.7} [558]	198 (28.7) {25.5,32.2} [689]	256 (31.9) {28.8,35.2} [802]	410 (37.0) {34.2,39.9} [1,109]	546 (38.5) {36.0,41.0} [1,419]	706 (40.3) {38.0,42.6} [1,754]	738 (41.5) {39.2,43.8} [1,780]	731 (41.8) {39.5,44.1} [1,750]	807 (39.2) {37.1,41.3} [2,058]	887 (37.6) {35.7,39.6} [2,356]	879 (34.2) {32.4,36.1} [2,569]	983 (33.6) {31.9,35.3} [2,927]	1,103 (32.1) {30.6,33.7} [3,432]	1,226 (31.0) {29.6,32.5} [3,953]	1,305 (31.0) {29.6,32.4} [4,207]
Age, mean (SD)	48.7 (11.1)	49.9 (11.0)	47.9 (9.8)	49.4 (10.3)	49.3 (10.8)	50.2 (10.5)	50.2 (10.7)	50.0 (11.0)	49.7 (10.8)	50.1 (10.7)	50.0 (10.7)	50.3 (10.8)	50.9 (10.7)	50.0 (10.8)	50.8 (10.8)
Number of males, n (%)	89 (55.3)	119 (60.1)	161 (62.9)	245 (59.8)	325 (59.5)	459 (65.0)	438 (59.3)	442 (60.5)	484 (60.0)	545 (61.4)	537 (61.1)	592 (60.2)	683 (61.9)	727 (59.3)	802 (61.5)
Ethnicity , n (%)															
White											683 (91.8)	919 (93.5)	1,049 (95.2)	1,154 (94.4)	1,224 (93.9)
Asian											20 (2.7)	22 (2.2)	25 (2.3)	37 (3.0)	30 (2.3)
Black											2 (0.3)	5 (0.5)	6 (0.5)	6 (0.5)	9 (0.7)
Other											7 (0.9)	6 (0.6)	8 (0.7)	7 (0.6)	12 (0.9)
Not stated											32 (4.3)	31 (3.2)	14 (1.3)	18 (1.5)	28 (2.1)
Deprivation IMD quintile , n (%)															
1 (least deprived)	15 (9.9)	10 (5.3)	30 (12.4)	44 (11.0)	55 (10.4)	79 (11.4)	64 (8.8)	73 (10.1)	92 (11.6)	79 (9.0)	87 (10.0)	100 (10.3)	142 (13.0)	157 (12.9)	142 (11.0)
2	24 (15.9)	33 (17.5)	31 (12.9)	66 (16.5)	71 (13.4)	79 (11.4)	107 (14.7)	84 (11.6)	106 (13.4)	146 (16.6)	120 (13.8)	151 (15.5)	166 (15.2)	168 (13.8)	153 (11.8)
3	22 (14.6)	40 (21.2)	40 (16.6)	71 (17.8)	96 (18.1)	121 (17.5)	115 (15.8)	154 (21.2)	117 (14.8)	138 (15.7)	157 (18.0)	161 (16.5)	181 (16.5)	204 (16.8)	236 (18.2)
4	39 (25.8)	37 (19.6)	52 (21.6)	78 (19.5)	109 (20.6)	148 (21.4)	148 (20.3)	153 (21.1)	176 (22.3)	207 (23.5)	221 (25.3)	195 (20.0)	235 (21.5)	294 (24.2)	317 (24.5)
5 (most deprived)	51 (33.8)	69 (36.5)	88 (36.5)	140 (35.1)	198 (37.4)	263 (38.1)	294 (40.4)	261 (36.0)	300 (37.9)	309 (35.2)	287 (32.9)	367 (37.7)	371 (33.9)	394 (32.4)	448 (34.6)
APACHE II Acute Physiology Score, mean (SD)	16.8 (7.7)	16.9 (8.1)	18.6 (8.0)	17.9 (7.8)	17.3 (7.2)	17.1 (7.5)	17.1 (7.7)	17.3 (7.3)	16.7 (7.5)	17.4 (7.3)	16.2 (7.1)	16.8 (7.1)	16.4 (6.6)	16.5 (6.9)	16.1 (6.6)
APACHE II score, mean (SD)	20.0 (8.1)	20.4 (8.5)	22.0 (8.5)	21.7 (8.5)	20.5 (7.6)	20.3 (8.0)	20.5 (8.2)	20.7 (7.8)	20.0 (8.1)	21.1 (7.8)	20.1 (7.6)	20.8 (7.6)	20.6 (7.2)	20.7 (7.5)	20.6 (7.0)
ICNARC physiology score, mean (SD)	24.5 (10.3)	26.7 (11.6)	27.2 (10.8)	26.7 (11.5)	25.0 (10.7)	24.8 (10.8)	24.7 (11.4)	25.0 (10.9)	24.2 (10.6)	24.7 (10.4)	23.5 (10.2)	24.5 (10.3)	24.0 (9.9)	24.0 (9.9)	23.2 (9.9)

Highest serum creatinine*, mean (SD)	191.5 (164.1)	181.2 (151.2)	180.2 (130.4)	186.7 (176.1)	177.2 (151.5)	179.2 (158.3)	171.6 (149.9)	170.5 (141.8)	168.7 (147.2)	169.6 (137.8)	162.5 (134.9)	174.7 (145.2)	170.5 (152.9)	174.9 (165.5)	161.4 (149.9)
Highest blood lactate, mean (SD)**											4.6 (4.4)	5.0 (4.7)	5.0 (4.5)	5.0 (4.7)	4.7 (4.5)

*Missing data for 27% of admissions

**Missing data for 14% of admissions

Table S8b: Alcohol related – Outcomes

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Critical care unit mortality, deaths (%) {CI} [N]	82 (50.9) {43.3,58.5} [161]	107 (54.0) {47.1,60.8} [198]	146 (57.0) {50.9,62.9} [256]	218 (53.2) {48.3,57.9} [410]	262 (48.0) {43.8,52.2} [546]	332 (47.0) {43.4,50.7} [706]	344 (46.6) {43.0,50.2} [738]	346 (47.3) {43.7,51.0} [731]	357 (44.2) {40.8,47.7} [807]	412 (46.4) {43.2,49.7} [887]	369 (42.0) {38.8,45.3} [879]	464 (47.2) {44.1,50.3} [983]	457 (41.4) {38.6,44.4} [1,103]	507 (41.4) {38.6,44.1} [1,226]	547 (41.9) {39.3,44.6} [1,305]
Acute hospital mortality*, deaths (%) {CI} [N]	104 (66.7) {58.9,73.6} [156]	129 (66.8) {59.9,73.1} [193]	170 (69.7) {63.6,75.1} [244]	271 (70.2) {65.5,74.6} [386]	357 (69.5) {65.3,73.3} [514]	447 (66.9) {63.3,70.4} [668]	441 (62.4) {58.7,65.9} [707]	454 (64.7) {61.1,68.1} [702]	483 (63.1) {59.6,66.4} [766]	530 (62.4) {59.1,65.6} [849]	493 (58.2) {54.9,61.5} [847]	591 (62.0) {58.9,65.0} [953]	625 (58.6) {55.6,61.5} [1,067]	689 (58.6) {55.8,61.4} [1,175]	729 (58.1) {55.3,60.8} [1,255]
Number of patients readmitted, n (%) [N]**	7 (11.9) [59]	5 (6.8) [74]	12 (13.8) [87]	27 (18.4) [147]	30 (12.5) [240]	38 (12.5) [304]	29 (8.3) [351]	24 (7.5) [320]	54 (14.4) [374]	36 (8.8) [410]	41 (9.8) [419]	33 (7.6) [437]	51 (9.1) [561]	65 (10.9) [596]	63 (9.7) [650]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S8c: Alcohol related – Resource use

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support															
Number, n (%)											633 (72.0)	679 (69.1)	757 (68.6)	811 (66.2)	880 (67.4)
Duration (All), median (IQR)											2 (0,5)	2 (0,6)	2 (0,6)	2 (0,5)	2 (0,5)
Duration (Receivers), median (IQR)											4 (2,8)	4 (2,8)	4 (2,8)	4 (2,8)	3 (2,8)

Basic cardiovascular support															
Number, n (%)											729 (82.9)	833 (84.7)	919 (83.3)	1,043 (85.1)	1,151 (88.2)
Duration (All), median (IQR)											3 (1,6)	3 (1,7)	3 (1,7)	3 (1,6)	3 (2,7)
Duration (Receivers), median (IQR)											4 (2,8)	4 (2,7)	4 (2,8)	3 (2,7)	4 (2,7)
Advanced cardiovascular support															
Number, n (%)											403 (45.8)	348 (35.4)	358 (32.5)	433 (35.3)	370 (28.4)
Duration (All), median (IQR)											0 (0,2)	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)
Duration (Receivers), median (IQR)											2 (1,4)	2 (1,4)	2 (1,4)	2 (1,3)	2 (1,4)
Renal support															
Number, n (%)											259 (29.5)	205 (20.9)	211 (19.1)	259 (21.1)	253 (19.4)
Duration (All), median (IQR)											0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)											3 (2,6)	3 (2,5)	4 (2,8)	3 (2,6)	3 (2,6)
Critical care unit length of stay															
All, mean (sd)	4.4 (6.5)	4.2 (6.0)	4.2 (5.7)	5.3 (6.9)	5.8 (8.5)	5.4 (7.4)	5.0 (6.7)	5.6 (7.8)	5.2 (7.9)	5.1 (6.6)	6.0 (8.0)	5.7 (7.3)	6.2 (8.5)	5.6 (7.0)	6.3 (8.6)
Unit non-survivors, median (IQR)	2.3 (0.9,6.8)	1.6 (0.6,5.0)	2.6 (1.1,5.6)	2.2 (0.7,6.3)	2.2 (1.0,6.8)	2.5 (0.9,6.1)	1.7 (0.6,5.3)	1.8 (0.7,5.9)	2.1 (0.7,5.8)	1.9 (0.8,5.2)	2.3 (0.7,5.8)	2.7 (0.8,6.1)	2.5 (0.9,6.3)	2.2 (0.9,6.0)	2.4 (0.9,6.6)
Unit survivors, median (IQR)	1.5 (0.8,4.2)	2.0 (0.9,5.9)	1.8 (1.0,3.5)	2.8 (1.0,8.4)	3.0 (1.2,7.8)	3.0 (1.2,6.9)	3.1 (1.2,6.9)	3.5 (1.5,7.7)	2.7 (1.4,7.0)	3.1 (1.7,7.8)	3.8 (1.7,8.6)	3.2 (1.6,7.8)	3.9 (1.8,9.3)	3.9 (1.7,8.4)	4.0 (1.8,8.9)
Acute hospital length of stay*															
All, mean (sd)	21.9 (28.1)	20.6 (39.4)	18.9 (24.2)	21.6 (29.6)	21.6 (27.2)	22.5 (28.7)	21.5 (28.7)	21.0 (24.8)	20.1 (25.7)	19.4 (24.4)	22.7 (33.4)	19.4 (22.7)	23.5 (28.0)	21.5 (28.0)	21.5 (24.7)
Unit non-survivors, median (IQR)	8.0 (3.0,14.0)	5.0 (2.0,14.0)	7.0 (3.0,14.0)	8.0 (3.0,17.0)	8.0 (3.0,21.0)	8.0 (4.0,17.0)	8.0 (3.0,17.0)	8.0 (3.0,17.0)	8.0 (2.0,16.0)	8.0 (3.0,15.0)	8.0 (3.0,19.0)	8.0 (3.0,16.0)	8.0 (3.0,18.0)	9.0 (3.0,17.0)	8.0 (3.0,18.0)

Unit survivors, median (IQR)	38.5 (14.5,62.0)	22.5 (14.5,36.0)	24.0 (13.0,48.0)	32.0 (13.0,51.0)	25.0 (15.0,45.5)	30.0 (13.0,53.0)	25.0 (14.0,42.0)	27.0 (15.0,46.0)	24.0 (12.0,42.0)	24.0 (12.0,39.0)	25.0 (13.0,42.0)	24.0 (13.0,39.0)	25.0 (14.0,45.0)	23.0 (12.0,40.0)	24.0 (12.0,44.0)

*Excluding readmissions

Table S9a: Non-alcohol related – Demographics and case mix

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Number of admissions, n (%) {CI} [N]	397 (71.1) {67.3,74.8} [558]	491 (71.3) {67.8,74.5} [689]	546 (68.1) {64.8,71.2} [802]	699 (63.0) {60.1,65.8} [1,109]	873 (61.5) {59.0,64.0} [1,419]	1,048 (59.7) {57.4,62.0} [1,754]	1,042 (58.5) {56.2,60.8} [1,780]	1,019 (58.2) {55.9,60.5} [1,750]	1,251 (60.8) {58.7,62.9} [2,058]	1,469 (62.4) {60.4,64.3} [2,356]	1,690 (65.8) {63.9,67.6} [2,569]	1,944 (66.4) {64.7,68.1} [2,927]	2,329 (67.9) {66.3,69.4} [3,432]	2,727 (69.0) {67.5,70.4} [3,953]	2,902 (69.0) {67.6,70.4} [4,207]
Age, mean (SD)	50.7 (14.3)	51.5 (14.4)	52.9 (13.3)	52.1 (13.4)	53.7 (13.7)	54.2 (13.8)	54.2 (14.0)	55.3 (13.3)	53.3 (13.7)	54.5 (13.8)	54.9 (13.5)	53.8 (13.2)	54.8 (12.8)	54.5 (12.7)	54.7 (13.3)
Number of males, n (%)	226 (56.9)	302 (61.5)	353 (64.7)	443 (63.4)	530 (60.7)	629 (60.0)	635 (60.9)	642 (63.0)	754 (60.3)	880 (59.9)	1,060 (62.7)	1,212 (62.3)	1,426 (61.2)	1,688 (61.9)	1,853 (63.9)
Ethnicity , n (%)															
White											1,296 (87.9)	1,702 (87.6)	2,108 (91.1)	2,419 (90.1)	2,605 (90.5)
Asian											84 (5.7)	108 (5.6)	98 (4.2)	125 (4.7)	139 (4.8)
Black											21 (1.4)	38 (2.0)	35 (1.5)	47 (1.7)	48 (1.7)
Other											16 (1.1)	31 (1.6)	33 (1.4)	46 (1.7)	49 (1.7)
Not stated											58 (3.9)	63 (3.2)	39 (1.7)	49 (1.8)	39 (1.4)
Deprivation IMD quintile , n (%)															
1 (least deprived)	43 (11.5)	64 (13.7)	69 (13.0)	93 (13.8)	115 (13.7)	141 (13.8)	136 (13.3)	138 (13.8)	163 (13.2)	208 (14.3)	237 (14.3)	268 (13.9)	280 (12.2)	334 (12.4)	347 (12.1)
2	62 (16.5)	76 (16.3)	75 (14.2)	76 (11.2)	128 (15.3)	175 (17.1)	175 (17.1)	150 (15.0)	196 (15.8)	273 (18.7)	272 (16.4)	320 (16.6)	351 (15.3)	387 (14.3)	449 (15.7)
3	72 (19.2)	75 (16.1)	99 (18.7)	135 (20.0)	143 (17.1)	189 (18.5)	173 (16.9)	172 (17.2)	197 (15.9)	248 (17.0)	319 (19.2)	323 (16.8)	439 (19.1)	515 (19.1)	523 (18.2)
4	72 (19.2)	97 (20.8)	103 (19.4)	154 (22.8)	177 (21.1)	193 (18.9)	208 (20.3)	205 (20.5)	276 (22.3)	289 (19.8)	345 (20.7)	407 (21.1)	491 (21.4)	610 (22.6)	648 (22.6)
5 (most deprived)	126 (33.6)	154 (33.0)	184 (34.7)	218 (32.2)	275 (32.8)	324 (31.7)	332 (32.4)	336 (33.6)	406 (32.8)	440 (30.2)	490 (29.5)	607 (31.5)	735 (32.0)	857 (31.7)	902 (31.4)
APACHE II Acute Physiology Score, mean (SD)	15.7 (7.8)	15.5 (8.1)	15.8 (7.4)	15.2 (7.6)	15.5 (7.5)	16.0 (7.6)	15.5 (7.4)	15.4 (7.5)	15.2 (7.2)	14.9 (6.9)	14.2 (6.7)	14.3 (6.7)	14.5 (6.5)	13.9 (6.4)	13.9 (6.3)
APACHE II score, mean (SD)	20.5 (8.7)	20.3 (8.7)	20.8 (8.1)	20.2 (8.4)	20.6 (8.3)	21.1 (8.4)	20.4 (8.3)	20.4 (8.4)	20.0 (8.0)	19.7 (7.6)	18.9 (7.5)	19.1 (7.4)	19.5 (7.3)	19.0 (7.2)	19.0 (7.2)
ICNARC physiology score, mean (SD)	22.1 (11.4)	22.3 (12.3)	22.6 (11.6)	22.0 (11.4)	22.6 (11.6)	23.1 (11.0)	22.5 (10.9)	22.4 (10.6)	21.6 (10.8)	21.3 (10.1)	21.1 (10.2)	21.6 (10.1)	21.7 (9.9)	20.7 (9.8)	20.5 (9.9)

Highest serum creatinine*, mean (SD)	170.6 (145.7)	163.0 (127.6)	153.7 (120.8)	156.8 (121.4)	156.3 (128.7)	166.2 (139.3)	155.3 (127.7)	154.9 (127.1)	152.8 (141.2)	149.0 (122.2)	152.1 (141.5)	161.3 (152.1)	152.4 (130.9)	144.2 (132.1)	142.1 (130.0)
Highest blood lactate, mean (SD)**											4.5 (4.4)	4.4 (4.3)	4.5 (4.2)	4.3 (4.2)	4.2 (4.0)

*Missing data for 26% of admissions

**Missing data for 13% of admissions

Table S9b: Non-alcohol related – Outcomes

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Critical care unit mortality, deaths (%) {CI} [N]	145 (36.5) {31.9,41.4} [397]	183 (37.3) {33.1,41.6} [491]	197 (36.1) {32.2,40.2} [546]	231 (33.0) {29.7,36.6} [699]	308 (35.3) {32.2,38.5} [873]	380 (36.3) {33.4,39.2} [1,048]	347 (33.3) {30.5,36.2} [1,042]	335 (32.9) {30.1,35.8} [1,019]	387 (30.9) {28.4,33.6} [1,251]	426 (29.0) {26.7,31.4} [1,469]	490 (29.0) {26.9,31.2} [1,690]	563 (29.0) {27.0,31.0} [1,944]	681 (29.2) {27.4,31.1} [2,329]	710 (26.0) {24.4,27.7} [2,727]	744 (25.6) {24.1,27.3} [2,902]
Acute hospital mortality*, deaths (%) {CI} [N]	193 (54.2) {49.0,59.3} [356]	233 (52.1) {47.5,56.7} [447]	245 (50.8) {46.4,55.3} [482]	297 (49.6) {45.6,53.6} [599]	387 (49.4) {45.9,52.9} [783]	473 (50.8) {47.5,54.0} [932]	473 (50.2) {47.0,53.4} [942]	456 (48.8) {45.6,52.0} [935]	501 (44.6) {41.7,47.5} [1,123]	579 (43.9) {41.2,46.6} [1,320]	656 (42.0) {39.5,44.4} [1,563]	772 (43.3) {41.0,45.6} [1,782]	955 (44.4) {42.3,46.5} [2,153]	1,006 (39.8) {37.9,41.7} [2,529]	1,058 (39.6) {37.7,41.4} [2,673]
Number of patients readmitted, n (%) [N]**	25 (12.8) [195]	30 (11.8) [254]	38 (13.8) [275]	60 (16.1) [372]	63 (13.4) [469]	72 (12.9) [556]	75 (13.0) [578]	60 (10.3) [580]	77 (10.8) [714]	103 (12.1) [848]	82 (8.1) [1,012]	113 (9.9) [1,144]	128 (9.5) [1,346]	157 (9.4) [1,675]	168 (9.4) [1,784]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S9c: Non-alcohol related – Resource use

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support															
Number, n (%)											1,216 (72.0)	1,343 (69.1)	1,585 (68.1)	1,778 (65.2)	1,826 (62.9)
Duration (All), median (IQR)											2 (0,4)	2 (0,5)	2 (0,4)	2 (0,4)	2 (0,4)
Duration (Receivers), median (IQR)											2 (2,6)	3 (2,8)	3 (2,6)	3 (2,7)	3 (2,7)

Basic cardiovascular support															
Number, n (%)											1,470 (87.0)	1,689 (86.9)	2,028 (87.1)	2,397 (87.9)	2,543 (87.6)
Duration (All), median (IQR)											3 (1,5)	3 (2,6)	3 (2,6)	3 (2,6)	3 (2,6)
Duration (Receivers), median (IQR)											3 (2,6)	3 (2,7)	3 (2,6)	3 (2,6)	3 (2,7)
Advanced cardiovascular support															
Number, n (%)											695 (41.1)	638 (32.8)	706 (30.3)	783 (28.7)	791 (27.3)
Duration (All), median (IQR)											0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)
Duration (Receivers), median (IQR)											2 (1,3)	2 (1,3)	2 (1,3)	2 (1,4)	2 (1,3)
Renal support															
Number, n (%)											443 (26.2)	375 (19.3)	403 (17.3)	476 (17.5)	494 (17.0)
Duration (All), median (IQR)											0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)											3 (2,6)	3 (2,7)	4 (2,7)	3 (2,6)	3 (2,6)
Critical care unit length of stay															
All, mean (sd)	3.6 (5.2)	4.4 (10.6)	4.8 (7.2)	4.7 (6.8)	5.2 (10.0)	5.0 (7.0)	5.0 (6.5)	5.1 (8.6)	5.3 (7.9)	5.2 (7.8)	4.9 (6.8)	5.5 (7.6)	5.5 (8.0)	5.4 (7.6)	5.4 (7.1)
Unit non-survivors, median (IQR)	1.6 (0.6,5.6)	1.6 (0.7,4.9)	2.1 (0.8,7.0)	2.7 (0.9,7.5)	2.4 (0.8,6.7)	2.0 (0.8,5.6)	2.7 (0.9,7.8)	2.3 (0.9,7.0)	2.6 (0.8,7.0)	2.0 (0.7,6.0)	2.2 (0.8,6.9)	2.3 (0.9,7.6)	2.4 (0.8,6.5)	2.7 (0.8,7.2)	2.7 (0.9,7.5)
Unit survivors, median (IQR)	1.8 (0.8,4.1)	1.6 (0.8,4.0)	2.0 (1.0,5.1)	1.9 (0.9,5.0)	2.1 (1.0,5.1)	2.5 (1.0,6.7)	2.3 (1.1,5.8)	2.4 (1.1,5.5)	2.4 (1.1,6.0)	2.6 (1.2,5.9)	2.5 (1.3,5.6)	2.9 (1.3,6.4)	3.0 (1.5,6.3)	2.9 (1.4,6.2)	2.9 (1.4,6.2)
Acute hospital length of stay*															
All, mean (sd)	21.5 (30.4)	23.0 (30.5)	27.4 (36.1)	25.0 (28.4)	23.7 (28.4)	23.5 (28.4)	25.1 (27.2)	25.4 (29.8)	25.4 (33.4)	22.9 (27.0)	23.4 (28.4)	24.1 (31.9)	23.7 (29.9)	23.5 (28.5)	22.9 (26.8)
Unit non-survivors,	8.0 (2.5,16.0	9.0 (2.0,19.0	8.0 (3.0,22.0	10.0 (3.0,21.0	9.0 (3.0,21.0	10.0 (3.0,20.0	12.0 (4.0,24.0	11.0 (4.0,22.0	9.5 (4.0,21.0	10.0 (3.0,22.0	10.0 (3.0,22.0	11.0 (3.0,22.0	10.0 (3.0,20.0	11.0 (4.0,23.0	11.0 (4.0,22.0

median (IQR)	)	)	)	)	)	)	)	)	)	)	)	)	)	)	)
Unit survivors, median (IQR)	19.0 (12.0,40.0)	19.0 (11.0,37.0)	25.0 (14.0,44.0)	22.0 (13.0,42.0)	21.0 (13.0,37.0)	21.0 (13.0,36.0)	23.0 (13.0,39.0)	21.0 (11.0,43.0)	20.0 (11.0,37.0)	19.0 (11.0,35.0)	18.0 (10.0,33.0)	19.0 (10.0,35.0)	18.0 (10.0,36.0)	18.0 (10.0,32.0)	17.0 (9.0,33.0)

*Excluding readmissions

Table S10a: Haemorrhage – Demographics and case mix

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Number of admissions, n (%) {CI} [N]	52 (3.7) {2.8,4.8} [1,419]	46 (2.6) {2.0,3.5} [1,754]	48 (2.7) {2.0,3.6} [1,780]	37 (2.1) {1.5,2.9} [1,750]	47 (2.3) {1.7,3.0} [2,058]	59 (2.5) {1.9,3.2} [2,356]	61 (2.4) {1.9,3.0} [2,569]	72 (2.5) {2.0,3.1} [2,927]	77 (2.2) {1.8,2.8} [3,432]	92 (2.3) {1.9,2.8} [3,953]	97 (2.3) {1.9,2.8} [4,207]
Age, mean (SD)	48.9 (11.6)	51.9 (11.0)	48.8 (13.9)	50.9 (10.7)	53.0 (13.8)	52.0 (14.0)	53.0 (12.3)	51.4 (13.8)	50.4 (12.6)	51.0 (11.5)	50.0 (13.3)
Number of males, n (%)	33 (63.5)	34 (73.9)	32 (66.7)	24 (64.9)	30 (63.8)	37 (62.7)	43 (70.5)	49 (68.1)	51 (66.2)	66 (71.7)	65 (67.0)
Ethnicity , n (%)											
White							49 (87.5)	65 (90.3)	68 (89.5)	77 (84.6)	85 (87.6)
Asian							0 (0.0)	3 (4.2)	2 (2.6)	2 (2.2)	3 (3.1)
Black							1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)
Other							0 (0.0)	0 (0.0)	1 (1.3)	2 (2.2)	3 (3.1)
Not stated							6 (10.7)	4 (5.6)	5 (6.6)	10 (11.0)	4 (4.1)
Deprivation IMD quintile , n (%)											
1 (least deprived)	7 (14.0)	2 (4.4)	5 (10.4)	5 (13.5)	4 (8.5)	9 (15.5)	10 (16.9)	10 (13.9)	10 (13.2)	12 (13.2)	15 (15.6)
2	7 (14.0)	4 (8.9)	8 (16.7)	5 (13.5)	9 (19.1)	9 (15.5)	9 (15.3)	5 (6.9)	15 (19.7)	11 (12.1)	14 (14.6)
3	7 (14.0)	5 (11.1)	4 (8.3)	7 (18.9)	5 (10.6)	9 (15.5)	17 (28.8)	13 (18.1)	11 (14.5)	15 (16.5)	18 (18.8)
4	11 (22.0)	14 (31.1)	15 (31.3)	4 (10.8)	13 (27.7)	11 (19.0)	8 (13.6)	22 (30.6)	18 (23.7)	22 (24.2)	25 (26.0)
5 (most deprived)	18 (36.0)	20 (44.4)	16 (33.3)	16 (43.2)	16 (34.0)	20 (34.5)	15 (25.4)	22 (30.6)	22 (28.9)	31 (34.1)	24 (25.0)
APACHE II Acute Physiology Score, mean (SD)	15.7 (7.1)	13.8 (6.4)	14.3 (7.2)	16.1 (8.5)	15.0 (7.1)	13.3 (5.9)	13.5 (5.9)	14.1 (7.4)	15.1 (6.3)	13.3 (6.4)	13.8 (5.4)
APACHE II score, mean (SD)	19.2 (8.3)	17.5 (7.5)	17.0 (8.2)	19.4 (9.6)	18.8 (7.7)	17.7 (6.4)	17.6 (7.4)	18.0 (8.1)	19.6 (6.9)	17.2 (7.2)	17.8 (6.3)
ICNARC physiology score, mean (SD)	22.4 (10.2)	21.1 (10.0)	20.5 (12.3)	25.8 (12.4)	22.1 (10.2)	21.8 (11.5)	21.8 (9.8)	22.6 (10.8)	21.8 (8.4)	21.9 (9.6)	22.9 (9.6)
Highest serum creatinine*, mean (SD)	117.6 (97.1)	148.0 (165.0)	123.1 (77.0)	145.2 (82.6)	116.5 (63.5)	137.2 (105.7)	140.4 (125.4)	147.3 (95.4)	137.6 (118.3)	138.8 (100.6)	107.4 (71.1)
Highest blood lactate, mean (SD)**							3.7 (3.3)	5.3 (5.9)	4.9 (3.4)	5.2 (5.1)	5.3 (5.1)

*Missing data for 32% of admissions

**Missing data for 13% of admissions

Table S10b: Haemorrhage – Outcomes

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Critical care unit mortality, deaths (%) {CI} [N]	19 (36.5) {24.8,50.1} [52]	17 (37.0) {24.5,51.4} [46]	21 (43.8) {30.7,57.7} [48]	14 (37.8) {24.1,53.9} [37]	19 (40.4) {27.6,54.7} [47]	19 (32.2) {21.7,44.9} [59]	14 (23.0) {14.2,34.9} [61]	26 (36.1) {26.0,47.6} [72]	23 (29.9) {20.8,40.8} [77]	26 (28.3) {20.1,38.2} [92]	32 (33.0) {24.4,42.8} [97]
Acute hospital mortality*, deaths (%) {CI} [N]	27 (54.0) {40.4,67.0} [50]	19 (44.2) {30.4,58.9} [43]	24 (51.1) {37.2,64.7} [47]	23 (62.2) {46.1,75.9} [37]	24 (54.5) {40.1,68.3} [44]	28 (49.1) {36.6,61.7} [57]	22 (36.7) {25.6,49.3} [60]	33 (50.0) {38.3,61.7} [66]	42 (58.3) {46.8,69.0} [72]	46 (51.7) {41.5,61.8} [89]	49 (54.4) {44.2,64.3} [90]
Number of patients readmitted, n (%) [N]**	5 (20.8) [24]	3 (12.0) [25]	1 (4.3) [23]	5 (22.7) [22]	1 (4.3) [23]	4 (12.1) [33]	2 (5.1) [39]	5 (15.6) [32]	4 (9.8) [41]	8 (14.5) [55]	7 (13.5) [52]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S10c: Haemorrhage – Resource use

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support											
Number, n (%)							46 (75.4)	54 (75.0)	57 (74.0)	73 (79.3)	82 (84.5)
Duration (All), median (IQR)							2 (0,4)	2 (1,5)	2 (0,7)	2 (1,4)	2 (1,5)
Duration (Receivers), median (IQR)							2 (2,5)	3 (2,7)	5 (2,9)	3 (2,5)	3 (2,6)
Basic cardiovascular support											
Number, n (%)							58 (95.1)	66 (91.7)	71 (92.2)	82 (89.1)	87 (89.7)
Duration (All), median (IQR)							3 (2,6)	3 (2,7)	3 (2,8)	3 (2,5)	3 (2,6)
Duration (Receivers), median (IQR)							3 (2,6)	3 (2,7)	3 (2,8)	3 (2,6)	3 (2,8)
Advanced cardiovascular support											
Number, n (%)							17 (27.9)	17 (23.6)	24 (31.2)	19 (20.7)	25 (25.8)
Duration (All), median (IQR)							0 (0,0)	0 (0,0)	0 (0,1)	0 (0,0)	0 (0,1)

Duration (Receivers), median (IQR)							2 (1,4)	2 (1,3)	2 (1,3)	2 (1,3)	2 (1,2)
Renal support											
Number, n (%)							10 (16.4)	14 (19.4)	9 (11.7)	9 (9.8)	8 (8.2)
Duration (All), median (IQR)							0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)							4 (2,10)	4 (2,5)	5 (4,12)	4 (3,6)	2 (2,4)
Critical care unit length of stay											
All, mean (sd)	4.9 (6.7)	4.4 (5.7)	4.6 (4.5)	4.7 (6.0)	4.5 (4.6)	4.1 (4.8)	4.3 (4.6)	4.8 (5.9)	5.9 (6.5)	4.0 (4.3)	5.0 (5.6)
Unit non-survivors, median (IQR)	3.2 (1.0,7.7)	2.4 (0.5,4.1)	3.6 (1.5,6.4)	1.1 (0.3,6.8)	3.1 (0.9,10.2)	0.9 (0.2,4.4)	2.0 (0.6,8.6)	2.0 (0.7,6.7)	3.6 (1.4,9.2)	1.2 (0.4,3.4)	1.6 (0.9,6.5)
Unit survivors, median (IQR)	2.1 (1.3,4.7)	2.5 (1.2,6.0)	2.6 (1.5,5.8)	3.2 (1.9,7.0)	2.1 (1.0,5.5)	2.7 (1.2,6.1)	2.1 (1.1,6.7)	3.2 (1.1,6.0)	4.0 (1.6,8.1)	3.0 (1.7,5.7)	4.0 (1.6,7.4)
Acute hospital length of stay*											
All, mean (sd)	19.1 (18.1)	17.0 (16.3)	20.6 (23.1)	18.6 (25.7)	21.5 (20.3)	21.0 (33.9)	20.6 (20.8)	19.1 (21.0)	23.3 (34.6)	22.3 (28.2)	21.0 (20.7)
Unit non-survivors, median (IQR)	8.0 (3.0,16.0)	5.0 (1.0,10.0)	6.0 (2.5,13.5)	8.0 (1.0,15.0)	14.0 (5.0,22.5)	8.0 (1.0,19.0)	8.0 (4.0,20.0)	8.0 (2.0,16.0)	14.5 (5.0,21.0)	10.0 (2.0,32.0)	13.0 (3.0,22.5)
Unit survivors, median (IQR)	21.0 (13.0,34.0)	24.5 (11.5,30.5)	24.0 (13.0,39.0)	23.5 (11.0,38.0)	21.0 (9.0,43.5)	15.0 (10.0,32.0)	17.5 (9.0,32.0)	18.0 (7.0,28.0)	18.0 (9.0,38.0)	19.0 (9.0,30.0)	18.0 (9.0,40.0)

*Excluding readmissions

Table S11a: Non-haemorrhage – Demographics and case mix

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Number of admissions, n (%) {CI} [N]	1,367 (96.3) {95.2,97.2} [1,419]	1,708 (97.4) {96.5,98.0} [1,754]	1,732 (97.3) {96.4,98.0} [1,780]	1,713 (97.9) {97.1,98.5} [1,750]	2,011 (97.7) {97.0,98.3} [2,058]	2,297 (97.5) {96.8,98.1} [2,356]	2,508 (97.6) {97.0,98.1} [2,569]	2,855 (97.5) {96.9,98.0} [2,927]	3,355 (97.8) {97.2,98.2} [3,432]	3,861 (97.7) {97.2,98.1} [3,953]	4,110 (97.7) {97.2,98.1} [4,207]
Age, mean (SD)	52.1 (12.9)	52.6 (12.8)	52.6 (12.9)	53.1 (12.7)	51.9 (12.7)	52.8 (12.9)	53.2 (12.8)	52.7 (12.5)	53.6 (12.3)	53.2 (12.3)	53.6 (12.6)
Number of males, n (%)	822 (60.1)	1,054 (61.7)	1,041 (60.1)	1,060 (61.9)	1,208 (60.1)	1,388 (60.4)	1,554 (62.0)	1,755 (61.5)	2,058 (61.3)	2,349 (60.8)	2,590 (63.0)
Ethnicity , n (%)											
White							1,930 (89.2)	2,556 (89.6)	3,089 (92.5)	3,496 (91.6)	3,744 (91.6)
Asian							104 (4.8)	127 (4.5)	121 (3.6)	160 (4.2)	166 (4.1)
Black							22 (1.0)	43 (1.5)	41 (1.2)	53 (1.4)	55 (1.3)
Other							23 (1.1)	37 (1.3)	40 (1.2)	51 (1.3)	58 (1.4)
Not stated							84 (3.9)	90 (3.2)	48 (1.4)	57 (1.5)	63 (1.5)
Deprivation IMD quintile , n (%)											
1 (least deprived)	163 (12.4)	218 (13.1)	195 (11.4)	206 (12.2)	251 (12.7)	278 (12.2)	314 (12.7)	358 (12.7)	412 (12.4)	479 (12.5)	474 (11.6)
2	192 (14.6)	250 (15.0)	274 (16.1)	229 (13.6)	293 (14.8)	410 (18.0)	383 (15.5)	466 (16.5)	502 (15.1)	544 (14.2)	588 (14.5)
3	232 (17.6)	305 (18.3)	284 (16.7)	319 (18.9)	309 (15.6)	377 (16.5)	459 (18.5)	471 (16.7)	609 (18.4)	704 (18.4)	741 (18.2)
4	275 (20.9)	327 (19.6)	341 (20.0)	354 (21.0)	439 (22.1)	485 (21.3)	558 (22.5)	580 (20.5)	708 (21.4)	882 (23.0)	940 (23.1)
5 (most deprived)	455 (34.5)	567 (34.0)	610 (35.8)	581 (34.4)	690 (34.8)	729 (32.0)	762 (30.8)	952 (33.7)	1,084 (32.7)	1,220 (31.9)	1,326 (32.6)
APACHE II Acute Physiology Score, mean (SD)	16.2 (7.5)	16.5 (7.6)	16.2 (7.6)	16.2 (7.5)	15.8 (7.4)	15.9 (7.2)	14.9 (6.9)	15.2 (6.9)	15.1 (6.6)	14.8 (6.6)	14.6 (6.5)
APACHE II score, mean (SD)	20.6 (8.0)	20.9 (8.3)	20.5 (8.2)	20.5 (8.1)	20.1 (8.1)	20.3 (7.8)	19.4 (7.5)	19.7 (7.5)	19.9 (7.3)	19.5 (7.4)	19.5 (7.2)
ICNARC physiology score, mean (SD)	23.5 (11.4)	23.9 (11.0)	23.5 (11.1)	23.4 (10.8)	22.6 (10.8)	22.6 (10.3)	21.9 (10.3)	22.6 (10.2)	22.5 (10.0)	21.7 (9.9)	21.3 (10.0)
Highest serum creatinine*, mean (SD)	165.8 (138.9)	172.0 (146.8)	162.5 (137.9)	161.5 (134.2)	160.0 (144.8)	157.4 (129.3)	156.1 (139.7)	166.0 (150.9)	158.7 (139.1)	153.9 (144.6)	148.9 (137.6)
Highest blood lactate, mean (SD)**							4.5 (4.4)	4.6 (4.4)	4.7 (4.3)	4.5 (4.3)	4.3 (4.2)

*Missing data for 26% of admissions

**Missing data for 13% of admissions

Table S11b: Non-haemorrhage – Outcomes

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Critical care unit mortality, deaths (%) {CI} [N]	551 (40.3) {37.7,42.9} [1,367]	695 (40.7) {38.4,43.0} [1,708]	670 (38.7) {36.4,41.0} [1,732]	667 (38.9) {36.7,41.3} [1,713]	725 (36.1) {34.0,38.2} [2,011]	819 (35.7) {33.7,37.6} [2,297]	845 (33.7) {31.9,35.6} [2,508]	1,001 (35.1) {33.3,36.8} [2,855]	1,115 (33.2) {31.7,34.8} [3,355]	1,191 (30.8) {29.4,32.3} [3,861]	1,259 (30.6) {29.2,32.1} [4,110]
Acute hospital mortality*, deaths (%) {CI} [N]	717 (57.5) {54.7,60.2} [1,247]	901 (57.9) {55.4,60.3} [1,557]	890 (55.6) {53.1,58.0} [1,602]	887 (55.4) {53.0,57.9} [1,600]	960 (52.0) {49.8,54.3} [1,845]	1,081 (51.2) {49.1,53.3} [2,112]	1,127 (48.0) {45.9,50.0} [2,350]	1,330 (49.8) {47.9,51.7} [2,669]	1,538 (48.9) {47.1,50.6} [3,148]	1,649 (45.6) {44.0,47.2} [3,615]	1,738 (45.3) {43.7,46.9} [3,838]
Number of patients readmitted, n (%) [N]**	88 (12.8) [685]	107 (12.8) [835]	103 (11.4) [906]	79 (9.0) [878]	130 (12.2) [1,065]	135 (11.0) [1,225]	121 (8.7) [1,392]	141 (9.1) [1,549]	175 (9.4) [1,866]	214 (9.7) [2,216]	224 (9.4) [2,382]

*Excluding readmissions

**Number of patients discharged to location within the same hospital, who were readmitted to ICU within the same hospital stay, for any reason.

Table S11c: Non-haemorrhage – Resource use

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Advanced respiratory support											
Number, n (%)							1,803 (71.9)	1,968 (68.9)	2,285 (68.1)	2,516 (65.2)	2,624 (63.8)
Duration (All), median (IQR)							2 (0,4)	2 (0,5)	2 (0,5)	2 (0,4)	2 (0,4)
Duration (Receivers), median (IQR)							3 (2,7)	3 (2,8)	3 (2,7)	3 (2,7)	3 (2,7)
Basic cardiovascular support											
Number, n (%)							2,141 (85.4)	2,456 (86.0)	2,876 (85.7)	3,358 (87.0)	3,607 (87.8)
Duration (All), median (IQR)							3 (1,5)	3 (2,6)	3 (2,6)	3 (2,6)	3 (2,6)
Duration (Receivers), median (IQR)							3 (2,6)	4 (2,7)	3 (2,7)	3 (2,6)	3 (2,7)
Advanced cardiovascular support											
Number, n (%)							1,081 (43.1)	969 (33.9)	1,040 (31.0)	1,197 (31.0)	1,136 (27.6)
Duration (All), median (IQR)							0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)

Duration (Receivers), median (IQR)							2 (1,3)	2 (1,3)	2 (1,3)	2 (1,3)	2 (1,4)
Renal support											
Number, n (%)							692 (27.6)	566 (19.8)	605 (18.0)	726 (18.8)	739 (18.0)
Duration (All), median (IQR)							0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Duration (Receivers), median (IQR)							3 (2,6)	3 (2,6)	4 (2,8)	3 (2,6)	3 (2,6)
Critical care unit length of stay											
All, mean (sd)	5.5 (9.6)	5.2 (7.2)	5.0 (6.6)	5.3 (8.3)	5.3 (8.0)	5.2 (7.4)	5.3 (7.3)	5.6 (7.6)	5.7 (8.2)	5.5 (7.4)	5.7 (7.7)
Unit non-survivors, median (IQR)	2.3 (0.9,6.8)	2.2 (0.8,6.0)	2.1 (0.7,6.8)	2.1 (0.8,6.5)	2.4 (0.8,6.1)	2.0 (0.8,5.7)	2.2 (0.8,6.5)	2.5 (0.9,6.9)	2.4 (0.8,6.4)	2.5 (0.8,6.6)	2.6 (0.9,7.1)
Unit survivors, median (IQR)	2.5 (1.0,5.7)	2.7 (1.1,6.8)	2.7 (1.1,6.2)	2.7 (1.1,6.3)	2.6 (1.2,6.3)	2.7 (1.3,6.5)	2.9 (1.4,6.4)	3.0 (1.4,6.8)	3.1 (1.6,7.1)	3.0 (1.5,6.8)	3.0 (1.5,6.9)
Acute hospital length of stay*											
All, mean (sd)	23.0 (28.3)	23.2 (28.8)	23.6 (28.0)	23.7 (27.9)	23.3 (30.9)	21.6 (25.8)	23.2 (30.4)	22.5 (29.3)	23.7 (29.2)	22.9 (28.4)	22.4 (26.3)
Unit non-survivors, median (IQR)	8.0 (3.0,21.0)	9.0 (3.0,18.0)	10.0 (3.0,21.0)	9.0 (3.0,19.0)	9.0 (3.0,19.0)	9.0 (3.0,19.0)	9.0 (3.0,21.0)	9.0 (3.0,20.0)	9.0 (3.0,19.0)	10.0 (3.0,20.0)	9.0 (3.0,20.0)
Unit survivors, median (IQR)	23.0 (14.0,40.0)	23.0 (13.0,42.0)	24.0 (13.0,40.0)	23.0 (13.0,44.0)	21.0 (11.0,39.0)	20.0 (11.0,36.0)	20.0 (10.0,36.0)	20.0 (11.0,36.0)	20.0 (11.0,39.0)	19.0 (10.0,35.0)	18.0 (9.0,36.0)

*Excluding readmissions